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CONTENTS OF PREVIOUS NUMBER

AUGUST, 1928. NUMBER 2

The Cerebrospinal Fluid of Premature Infants, with Special Reference to Intracranial Hemorrhage and Pigmentation. Jerome Glaser, M.D., Chicago.

The Volume of the Blood: II. The Volume of the Blood and Concentration of Crystalloids and Electrolytes in Dehydration and Edema. Dan C. Darrow, M.D., St. Louis, and Thomas E. Buckman, M.D., Jacksonville, Fla.

Factors in the Decay of Teeth. Louise O. Kappes, M.D., Rochester, Minn.

A Possible Causal Factor of Food Allergy in Certain Infants. Bret Ratner, M.D., New York.

The Influence of Feeding on Certain Acids in the Feces of Infants: II. The Effect of an Excess of Lactose in Breast Milk and in Modified Cow's Milk, with Observations on a Parenteral Infection. Jesse R. Gerstley, M.D.; Chi Che Wang, Ph.D.; Ruth E. Bowden, M.S., and Agnes A. Wood, B.S., Chicago.

Blood Fat in Diabetic Children. Gladys L. Boyd, M.D. (Tor.), Toronto.

Rickets in Dogs as Probably Related to Sex. Charles R. Stockard, Ph.D., M.D., New York.

Pyuria in Children: The Use of the Cystogram. Charles F. McKhann, M.D., Boston.

Hemorrhage of the Suprarenals in the New-Born Infant: Diagnosis and Therapy. M. A. Goldzieher, M.D., and H. M. Greenwald, M.D., Brooklyn.

Case Reports:

Pterygium Colli Congenitum (Congenital Webbing). M. De Bruin, M.D., Amsterdam, The Netherlands.

Acrodynia (So-Called): A Study of the Pathology. James W. Kernohan, M.B., and Roger L. J. Kennedy, M.D., Rochester, Minn.

Vincent's Infection of the Nose: Report of a Case. Harold I. Shulman, M.D., Boston.

Progress in Pediatrics:

Conditions Leading to Prescoliosis: A Problem in Prophylaxis. A. Steindler, M.D., Iowa City.

Pediatric Biographies:

Thomas Phaer. John Ruhräh, Baltimore.

News and Comment.

Abstracts from Current Literature.

Society Transactions:

American Pediatric Society (First and Second Sessions).

New York Academy of Medicine, Section of Pediatrics.

Book Reviews.

Directory of Pediatric Societies.

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VOLUME 36 SEPTEMBER, 1928 NUMBER 3

PERMANENT RECORDS OF GROWTH AND NUTRITION OF CHILDREN *

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AND
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For the purpose of studying the rapid developmental changes which take place in growing children, we have been impressed with the desirability of having a method which would combine three essential characistics: first, a record which would possess permanency; second, a type of record which would permit actual visualization of the child, and finally, a record which would make possible the securing of comparative measurements. A photographic method suggested itself as a possible means of combining these characteristics and in addition of affording a method of accomplishing these results with great rapidity.

Visualization has impressed us as one of the most desirable of these characteristics, since a visual picture of a child conveys at once a definite idea of the nutritional status, whereas figures alone do not call forth a definite mental picture. The most accurate method of visualization, in our opinion, is through the agency of a stereoscopic photograph which makes possible a complete mental recreation of a child. In order to make the study more complete, it was desirable to have both anterior and lateral views of the children. This was accomplished by means of mirror photography. A large plane mirror of plate glass, 66 by 24 inches, was mounted in a frame which was placed at an angle of 45 degrees to the mesial plane of the child. This gave a reduced lateral view of the child in the negative. By this method, it was possible to obtain two views at the same time: an anterior and a reflected (hence reduced) lateral view. With the use of the stereoscopic camera, four images were thus obtained simultaneously.

METHOD OF SECURING MEASUREMENTS

The problem of securing measurements from photographs offered considerable difficulty for a time. The first method tried was that of constructing a screen about 3 feet by 6 feet with meshes of 1 sq. cm. Fine piano wires were stretched horizontally and vertically across a steel frame. They were placed exactly 1 cm. apart and made taut by means of pegs and a key. The tension of the wires, however, bent the frame, and little

* Received for publication, May 17, 1928.

* From the Department of Vital Economics, University of Rochester.

inaccuracies in spacing became apparent when a number of wires were tightened. This method, therefore, did not appear feasible, and certainly it did not possess sufficient accuracy. Next, an attempt was made to rule a centimeter scale on a large piece of cardboard for the purpose of securing a reduced scale on a negative which could be superimposed on the negatives of the children for measuring purposes. This, again, proved to be simpler in theory than in execution, for no one could be found who could rule such a large scale with sufficient accuracy to permit its use for measuring purposes. The method which was finally adopted consisted in accomplishing by photography what could not be done by hand, i.e., instead of making a large scale to be placed either in front of the child (e.g., the transparent or wire scale) or in the same position as

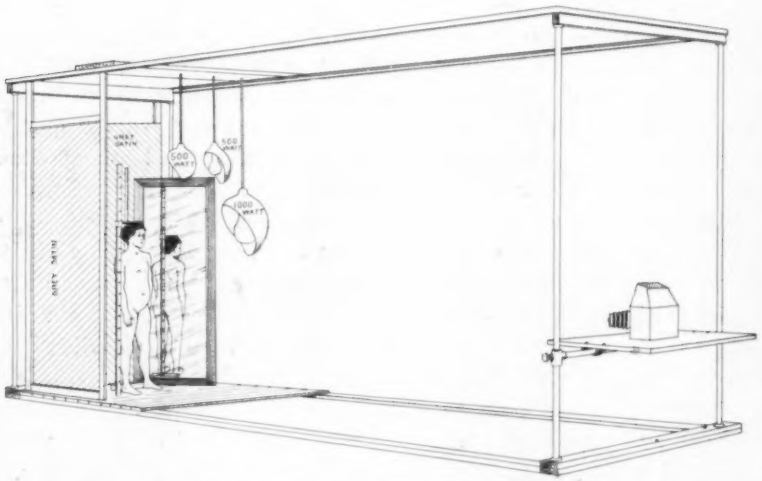

Fig. 1.—The method of illumination and of photographing simultaneously frontal and lateral views of the child. The camera can always be kept at the same distance from the subject and always at the same height. Dimensions of frame are given in the text.

the child (e.g., the opaque or ruled scale) at the time of photographing, a scale was photographed as a part of the picture.

It is clear that some sort of scale must be used in the plane in which the child is photographed in order to show the exact scale of reduction. The reduction of the child was about ten diameters; so it became necessary to find some sort of scale which would be plainly visible in this reduced picture. A surveyor's scale suggested itself, and satisfactory results were obtained with a Chicago Rod Ribbon, no. 350, style F graduation, made by the Chicago Steel Tape Company, Chicago. Two of these paper-cloth ribbons were used by cementing them with shellac to two flat pieces of iron of proper length, which served as supports. These ribbons are graduated in meters, tenths and hundredths, numbering up. Alternate centimeters are indicated by black squares 1 cm. on a side; fifth and tenth

centimeter divisions are indicated by longer marks, the decimeters being numbered. This type of scale is plainly visible in the negative. One of these scales was placed in the transverse plane and served as the basis for making measurements of the frontal silhouette of the negative. In order to measure the lateral silhouette, a second scale was placed behind the child in the mesial plane. This appears as a reduced scale in the lateral view.

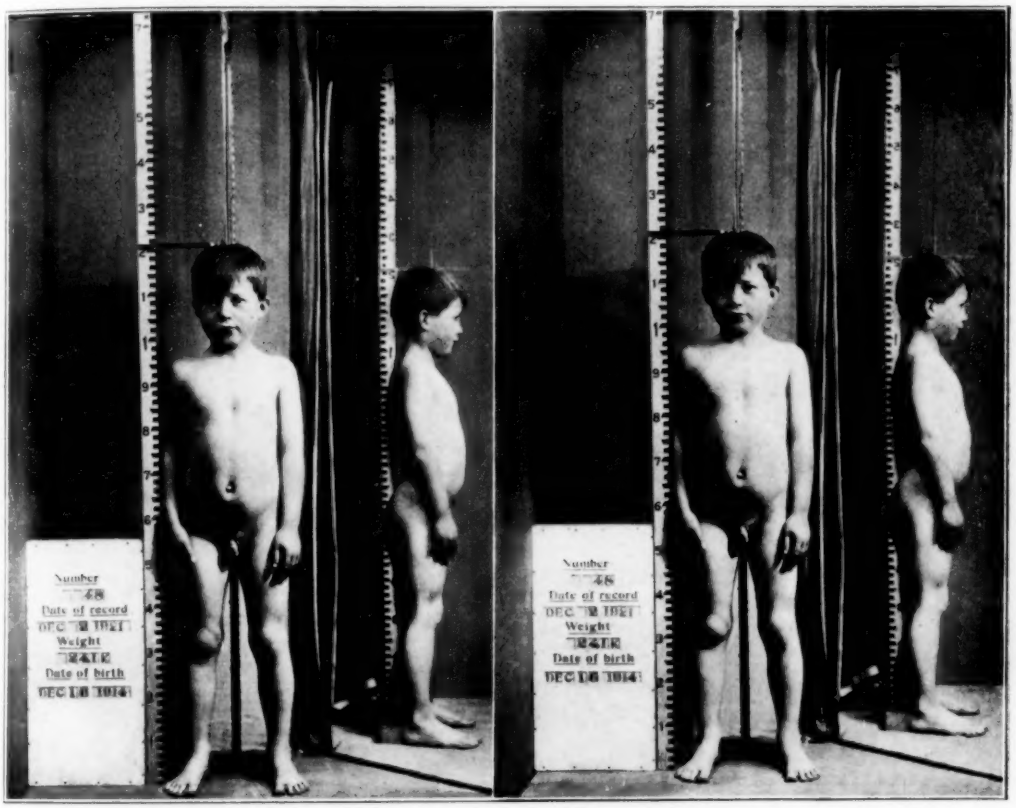

Fig. 2.—Stereoscopic picture showing front (direct) and lateral (reflected) views with their respective scales and the record of date of birth, date of picture, weight in kilograms and serial number of the subject.

Standardization of Negatives.—The basic idea which we had in mind in this work was that of devising an apparatus which would standardize all of the conditions under which the records were made so that the child could be placed in the apparatus at stated intervals and photographed. This involved primarily the standardization of the position of the child, the distance between the child and the camera, and finally the lighting conditions.

The child was placed in relation to two vertical iron rods, one of which supported at the bottom a block of wood 6 inches long and each of

which supported a metal bar projecting from it and joining that from the other rod in the form of a carpenter's square, which could be moved throughout the entire length of the rods and fastened in any given position so as to give the height of the subject. On each rod was pasted one of the metric scales previously described, so that one of them was reflected in the mirror. The other metric scale was placed to the right of the child, so that it nearly touched the right arm. The scale behind the child appeared in the lateral view and the one to the right appeared in the front view.

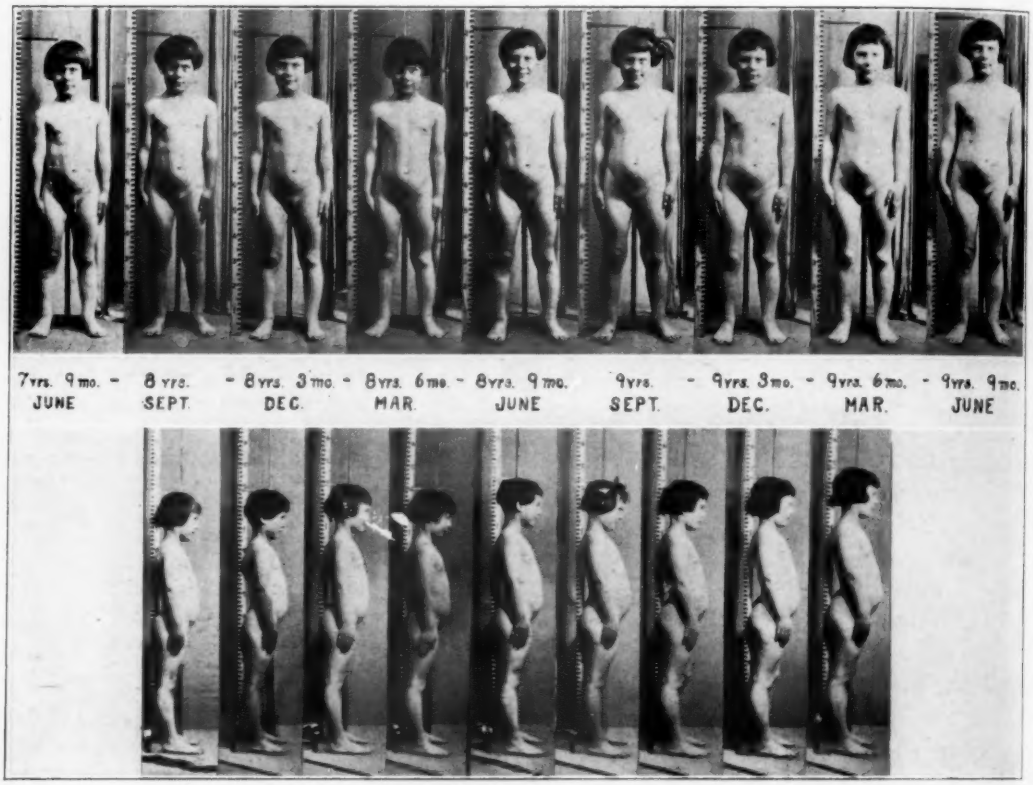

Fig. 3.—A short-stout type of girl, showing clearly the persistence of type and general morphologic features through two years, from 7 years and 9 months to 9 years and 9 months. Slight variations in the position of the feet do not invalidate the measurements of height.

Posture.—Fixation of the child was accomplished by placing the heels against the wooden block, and the sacrum, the spine between the scapulae and the occiput against the vertical rod. (This position fixed the spine and gave a slight spread to the legs so that the outlines of both legs could be plainly made out in the negative.) The position of the head was secured by the usual anthropometric method of tilting it so that the eyes were in the horizontal plane passing through the external auditory meatus. The right-angled square sliding on the measuring rods was lowered until it rested on the vertex (this is below the hair outline

whenever there is much hair on the head). The square was then fastened with a set-screw, and points on the square indicated on both measuring scales the height of the subject.

The arms were placed at the sides with the hands resting lightly on the thighs in such a manner as to leave the outline of the thigh unobscured in the lateral view.

Distance of Lens.—So long as the metric scales were photographed with the child, any desirable distance between the object and the lens could be used since

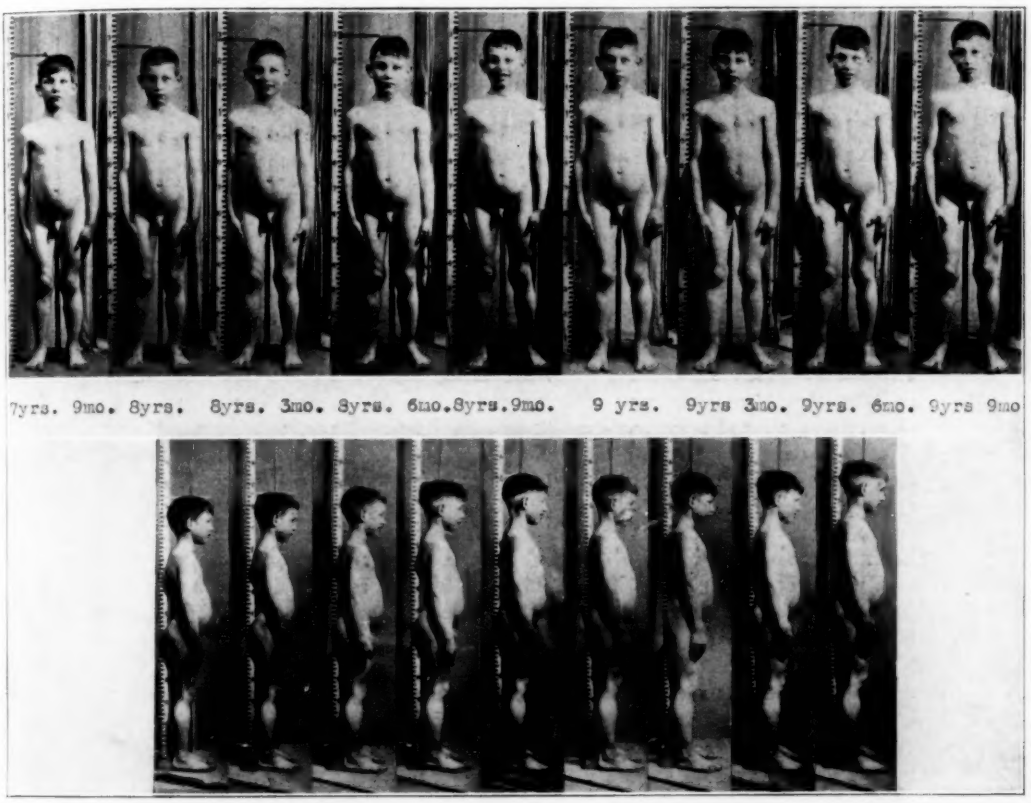

Fig. 4.—A medium-slender boy photographed at the same intervals over the same range of age as the girl in figure 3. There is an apparent acceleration of growth in height from March to June each year. Compare also the previous picture. It is not certain, however, that the camera was exactly the same height throughout.

all measurements made on the negatives are referred to the scales for their values. However, unless a constant distance was maintained, it would be necessary to construct separate measuring screens for different negatives. One great advantage in standardizing the distance lies in the fact that direct comparisons can be made between the numerous negatives of the same child made at different times, by direct superimposition. In this way the process of growth is shown in a

startling manner (figs. 3 and 4). When two negatives made a year apart are superimposed, the child can be seen completely surrounding the outline of its former self.

For the purpose of standardizing the lens-to-child distance, a portable and collapsible framework of wood and iron was constructed. This consisted of a rectangular base 12 feet long and 28 inches wide, built of two-by-fours, resting on the 4 inch side. Four uprights 8 feet high were bolted to this at the corners. A frame of 1½ inch angle iron of the same dimensions as the base rested on the four uprights. The fixtures used in the lighting system were bolted to this overhead iron frame, and the various backgrounds were attached to it. The backgrounds were of gray sateen stretched across wooden frames of proper size, and these frames, in turn, were hooked to the base and the upper support. The entire apparatus was held together with six bolts so that it could be completely assembled in a few minutes. The camera was attached to a small platform 15 by 15 inches which was secured to the iron pipes, 1¼ inches in diameter, which formed the uprights at one end of the apparatus. Thus when the apparatus was assembled, all of the distances were automatically standardized. Since this was true, and also since the child always stood in exactly the same place, the only variable factor in this system was the child itself.

Lighting Conditions.—The whole question of rapidity in obtaining these photographic records depends on having a source of light which is efficient as regards intensity and also one which is not variable. Daylight is ideal as far as intensity is concerned, but owing to the fact that it is so variable it could not be employed for the present purpose. An artificial lighting system was resorted to in order to overcome variations in intensity which otherwise would be unavoidable. Our system utilized three powerful "Daylight Mazda" lamps, and the work was done in a room from which all daylight was excluded. Two 500 watt lamps, one on either side and 14 inches below the upper frame, were used to illuminate the upper portion of the child, and a single 1000 watt lamp, 29 inches below the upper frame, placed on the left, was used to illuminate the lower part of the child. Each of these lamps was provided with a large reflector, lined with white porcelain, placed at an angle of 45 degrees. This type of reflector is in common use for illuminating commercial signs. The reflectors served to shield the camera lenses and at the same time to concentrate light on the subject. Stronger illumination was used on one side in order to give plasticity to the negatives, thus relieving the flatness which otherwise would result. Sufficient heat was generated by the lamps to keep the subjects warm during the placing and photographing.

By the foregoing methods, we have secured at regular intervals (three months) stereoscopic negatives showing the growth of upward of 150 children up to 15 years of age, covering a period of two years for each child. Each half of each of these negatives contains a frontal and a lateral silhouette made simultaneously. Incorporated in each of these silhouettes is its proper metric scale and on each can be superimposed a measuring screen made with any desirable unit of measure. By the use of the stereoscope or by the employment of stereoscopic projection, complete visualization of each of these children is possible (fig. 2). In the case of stereoscopic projection, by projecting to scale, accurate life size reproduction of the child is possible.

Camera.—The camera employed for this work was the stereoscopic Graflex, 5 by 7, made by the Folmer & Schwing Division of the Eastman Kodak Company of Rochester, N. Y. A magazine cut film holder was used so that twelve exposures could be made in rapid succession. The lenses were matched Bausch & Lomb Zeiss Tessar, Series II B, 3¼ by 4¼ inches, used at an aperture of f8. The

slowest rated instantaneous exposure with this type of outfit is 1/5 second, and that is the one used in this work. With the lighting arrangements previously described, this length of exposure was found to be sufficient.

Development of Negatives.—Eastman Portrait film, par speed, 5 by 7, was used in this work. For development, the tank system, time and temperature factors being used, was employed. The films were loaded into wire carriers by means of a loading fixture, and two dozen could be carried at a time. With the use of the tank factorial system, great speed and accurate control were secured, and the process of development was made almost automatic. After being loaded into the carriers, the films were carried through all of the operations—developing, fixing, washing and drying—without the necessity of being handled again until finished. This method of rapid, simple and accurate development is of paramount importance in handling the large number of negatives which were made.

Fitting Measuring Screens.—The impossibility of making a full sized measuring screen, either opaque or transparent, has been commented on previously. By the following method it was found to be a simple matter to fit a measuring screen directly to the negative. A piece of millimeter paper was placed in front of the lens of a camera arranged for copying, and one of the negatives was held against the ground glass screen. The camera lens was moved until the lines of the millimeter paper corresponded with any desired lines of the metric scale appearing in the negative, e. g., 1 mm. could be made to correspond to 1 cm. of the scale of the negative, 2 cm., or any desired division. As a matter of practice, instead of using a single division of the millimeter paper, we used 100 divisions, thus making it simpler and more accurate to match the millimeter paper to the scale on the negative. When an accurate correspondence was secured, by careful measurement a negative was made of the reduced millimeter paper and this could be used in front of the negative of the child, thus supplying ordinates and abscissas to scale for lantern slides or for printing on paper. A separate scale had to be made for the lateral view of the child, since this was a mirror image and hence reduced in size. The magnitude of this reduction was indicated by the metric scale appearing in the mirror image.

Stereoscopic Projection.—Stereoscopic projection was accomplished by the use of a double stereopticon (Model BB, Bausch & Lomb Optical Company, Rochester, N. Y.), complementary color filters being used. Two separate positives were made from the two portions of the double negative—one representing the right eye image and the other representing the left eye image. These were thrown on the screen through the two filters, one of red and the other blue-green, and the separation was made by the observer wearing spectacles made of lenses of the same filters. Absolute life size and realistic reproduction of the child was secured in this manner.

Identification.—Each child was given a number, and this number was used at each subsequent period. By means of a recorder made of heavy cardboard, 15 by 20 inches, with a series of openings, behind which were tapes running in grooves and bearing figures and letters, the following data were rapidly set up for each child by pulling the tapes into proper positions: number of child, date of birth, date of negative and weight of child. The recorder was set near the child and photographed with the child so that all of these data appeared on each negative.

COMMENT

As these records are, in the true sense of the word, actual recreations, they give a truer impression of the children at the

time when the records were made than can be given by any amount of description, either verbal or written. The lens can be made to see more than the eye records and possesses the supreme advantage of producing a permanent record which can be kept and studied at any future time. Many details which are missed in a casual examination are noted in studying the photographic records. The method which we have used in studying the growth and nutrition of children might be described as an extreme example of slow motion photography in which the time interval between successive negatives was lengthened to three months, and it is sufficient to get the child still for one-fifth second each three months.

In the course of studies in human constitution which have been in progress for several years at Columbia University and the Presbyterian Hospital in New York, Draper and his co-workers have been impressed with a fact which we have long had in mind in regard to the value of photographs in morphologic studies. The following statement appears in one of their articles on "Clinical Anthropometry":

> One other matter of interest has come to our attention; namely, the extreme accuracy with which the eye detects slight differences of morphology. In fact, we can often observe with the eye small anatomic differences which escape the most carefully made linear measurements and their ratios. Doubtless, this greater sensitiveness of the eye depends on the fact that small differences in surface area or mass are more easily appreciated than are similar small differences between units of one linear dimension.

USES FOR THIS METHOD OF STUDY

Important uses for this method of study which have come to our attention are: first, for form study; second, for nutritional study, and finally, for purposes of measurement and the study of growth correlations.

Form Study.—One of the chief uses of the method is to furnish material for morphologic study. As was pointed out before, slight developmental defects are most readily detected by the eye—and particularly through the study of stereoscopic photographs. Characteristic facies—as, for example, the adenoid facies—are quickly noted; endocrine disturbances affecting the growth of the skeleton and the deposition of body fat are caught; unusual postures are readily seen. For example, the marked lumbar lordosis of some children is in marked contrast to the almost complete absence of the lumbar curve of the spine in others.

Nutritional Study.—A stereoscopic photograph offers the best method of arriving at conclusions regarding the general nutritional condition of a child. It may be said to be quite as good as direct examination of the child. It may form the basis for many important inferences in regard to the health of the child. Consecutive standardized stereoscopic pho-

tographs offer one of the most satisfactory methods of following the nutritional status of children over long periods of time.

Measurements.—By means of accurate measuring apparatus such as the Lucas coordinate comparator manufactured by the Cambridge and Paul Instrument Company, practically unlimited refinement is possible in measuring the anterior and lateral silhouettes directly on the negative. Measurement under magnification by projection of the negatives on a smooth screen can also be carried out. Studies of the surface area of these silhouettes can be made by the use of a planimeter for rapidly calculating the areas of irregular surfaces. By the use of measurements of individual parts, it is hoped that correlations can be found between the growth of certain parts and other factors such as height and weight. Inspection of these negatives by superimposing them has brought out differences in the relative rates of growth of legs and trunk, for example. Individual variations and possible sex differences of relative rates also should be brought out by this method of study.

By placing the negatives over a translucent screen and magnifying them with a large reading glass, numerous measurements can be made with accurate calipers. For each particular region the graduations on the measuring tape of the appropriate view nearest to the part measured is compared with the caliper measurement. In practically all of the negatives examined the following measurements can be read off the front and lateral views, respectively, in this manner; front view, greatest width of face, narrowest diameter of neck, suprasternal notch to measuring bar on top of head, width of chest at level of nipples, narrowest diameter of waist, suprasternal notch to umbilicus, suprasternal notch to symphysis, greatest width of hips, greatest diameter of thigh, same for leg, length of leg, symphysis to ankle and others; in the lateral view, sagittal length of head, length of arm to elbow, greatest diameter of arm, depth of chest at level of nipples, patellar notch to bottom of foot, length of foot, etc.

Anthropometrists will object to the use of measurements which do not begin and end with some feature of the skeleton, and perhaps for comparative measurements in different subjects such features are the most reliable. But for observing relative rates of growth in the same child, other anatomic features can be utilized to advantage. A considerable number of such measurements have been made, but the report of these will be reserved for another paper.

For comparison, two figures are shown giving nine different exposures of the same child at a three months' interval in each case. For measurements, one of the stereoscopic pairs of negatives only is used so that any scratches caused by the calipers are confined to this one, the other being reserved for printing and mounting in the manner shown in figures 3 and 4.

UVEOPAROTID FEVER AS A MANIFESTATION OF MIKULICZ'S SYNDROME *

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AND
ALEXANDER J. SCHAFFER, M.D.
BALTIMORE

During 1905 and 1906, Heerfordt had the opportunity of observing three patients in the Copenhagen City Hospital, each of whom presented so similar and so striking a clinical picture that in 1909 he ventured to describe the condition as a hitherto unrecognized clinical entity. There were three essential and outstanding features in these cases: enlargement of the parotid glands lasting several months and thus running a relatively chronic course in contrast with the acute swelling in epidemic parotitis; an ocular inflammation involving the uveal tract, and a long continued fever of low degree corresponding with the subchronic course of both the iridocyclitis and the parotitis. In two of the three patients there were cerebrospinal paralyses. For this symptom-complex, Heerfordt proposed the descriptive title febris uveoparotidea subchronica, thus emphasizing the three chief characteristics and the course of the disorder.

Heerfordt's [1] communication was followed by numerous case reports of a similar nature and provoked much discussion of interest and value to both internists and ophthalmologists. It is curious to note that these contributions are chiefly German and Scandinavian. Rarely is there an English report, and only once is there an American reference to the disorder which, in the literature, either bears the originally proposed title or is alluded to as Heerfordt's disease or simply, uveoparotitis. As the disorder has received such scant attention in this country, and since its recognition needs to be stimulated and attention drawn to the spectacular effect of radiotherapy on the parotid tumor as well as on the ocular lesion, the following case of Heerfordt's syndrome is reported.

REPORT OF A CASE

History.—W. S.,[2] a white boy, aged 12, was admitted to the Harriet Lane Home on March 27, 1923, because of "sore, red eyes, fever and enlarged glands."

There was no family history of tuberculosis. With the exception of the usual diseases of childhood, the patient had enjoyed excellent health until the onset of the present disorder. Two years previously, he had had an attack of mumps.

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* Received for publication, May 17, 1928.

1. Heerfordt: Arch. f. Opth. **70**:254 (April) 1909.

2. We wish to thank Dr. Edwards A. Park for his kind permission to use the Harriet Lane Home records for this case.

In the latter part of December, 1922, three months before admission, the child returned from school complaining of headache. The temperature registered 103 F. He remained in bed a week with fever, and then returned to school, but a daily afternoon rise in temperature of from 100 to 101 F. persisted. On Feb. 26, 1923, the left eye appeared "quite red," and about a week later his mother observed that the pupil of this eye was irregular. With the lapse of another week, namely, about the end of the second week of March, the right eye became involved, and at the same time a swelling was noticed in the front of and below the left ear. A few days later a similar swelling appeared on the right side. These enlargements increased steadily in size until the time of admission on March 27, 1923.

Physical Examination.—On this date the boy did not seem ill and appeared well nourished and well developed, weighing 74½ pounds (33.8 Kg.). The parotid glands were markedly enlarged, projecting as huge masses from both sides of the face in the typical position: before, below and behind the ears. The lacrimal, submaxillary and sublingual glands were not increased in size. A few small lymphatic glands were palpable in the posterior cervical triangles, in the axillae and in the groins. On deepest inspiration, the tip of the spleen could be felt. The hepatic edge was not palpable. Examination of the lungs proved negative: the percussion note was resonant, and there were no adventitious sounds. Cardiac dulness was not increased; the heart sounds were clear. Roentgenologic examination of the chest confirmed the clinical observations; the apexes were clear, and there was no undue enlargement of the mediastinal glands. The tonsils had been removed seven years previously; the rhinopharyngeal examination was negative. The teeth were in good condition.

The conjunctiva of each eye was slightly injected; the pupils were widely dilated as the result of a mydriatic instillation. At this time Dr. Allen Woods furnished the details of an ophthalmologic examination.

In the right eye there were some deposits on the posterior corneal membrane in the lower portion of the cornea. The vitreous was clear. The disk was flat and the neuroretinal borders were obscured. There was a good deal of subretinal edema, and the retina was decidedly pale near the disk. The veins were somewhat overfilled.

In the left eye there were deposits on the posterior corneal membrane in the lower half of the cornea. There were some vitreous opacities. The disk was flat but blurred. Above the disk just below the vein there was a whitish area which seemed to be a deep choroidal exudate.

Diagnostic intradermal injections of tuberculin up to 5 mg. produced no reaction.

The red blood cells numbered 4,352,000; hemoglobin, 82 per cent; white blood cells, 5,400. The differential count (200 cells) showed: Wilson stain; polymorphonuclears, 61.5 per cent; polymorphonuclear eosinophils, 2.5 per cent; polymorphonuclear basophils, 0 per cent; large lymphocytes, 16 per cent; small lymphocytes, 10 per cent; mononuclears, 6 per cent; transitionals, 4 per cent. The cells in smear appeared normal. The platelets were normal in number and appearance. The Wassermann reaction was negative.

Treatment and Course.—The patient remained in the Harriet Lane Home three weeks, being discharged on April 19, 1923. During his stay in the hospital his condition changed little. The swollen parotid glands increased somewhat in size; the ocular condition continued unaltered, the temperature ranged from 97.2 to 100 F.; the weight remained stationary (fig. 1).

On April 25, 1923, an application of radium was made to the swollen right parotid gland under the direction of Dr. Curtis Burnam of the Howard A. Kelly

Sanitarium. The dose was 2 Gm. hours' irradiation screened with 1 mm. brass and 1 mm. lead at a distance of 5 cm. Five days later, it was noted that the right parotid tumor had diminished in size.

On May 1, 1923, the enlarged left parotid was similarly treated. On May 3, 1923, the observation was made that "whereas before radiation the mouth could scarcely be opened because of the impediment created by the swollen parotid glands, now the distance between the margins of the teeth can be enlarged by effort to 2.5 cm. He weighs 80¾ pounds, a gain of 6¼ pounds during the past two weeks."

On May 15, 1923, though both parotid tumors had diminished markedly in size, they were treated simultaneously with the same dosage of radium and with a similar technic. Thereafter, improvement proceeded uninterruptedly (fig. 2).

A B

A, photograph taken April 24, 1923, shows striking swelling of the parotid glands and closure of the eyes due to photophobia. *B*, photograph taken May 31, 1923, two weeks after the third application of radium. The complete subsidence of the parotid swelling and the total absence of photophobia should be noted.

When seen June 15, 1923, the boy weighed 85½ pounds (38.8 Kg.); a gain of almost 5 pounds (2.3 Kg.) during the past month. The parotids were no longer visible (fig. 2). Dr. Harry Friedenwald reported the ocular condition as follows: "The eyes show no external evidence of trouble; there is no congestion of the eyeballs. Pupils are round and equal; the corneae appear clear. With the magnifying glasses, however, there are a number of fine infiltrates in both corneae with a few fine deposits, the vestiges of the previous iritis. The vitreous in both eyes contain very fine dustlike opacities which are likewise the result of the above mentioned inflammation. The optic disks are exceedingly hyperemic, blurred in outline but show no swelling. The retinal arteries and veins are full but not beyond normal limits. There are no hemorrhages.

"The tests of vision show normal in both eyes (20/15). The fields of vision are quite normal both for form and color and the blind spots of Marriotte are not enlarged."

On Jan. 4, 1924, the only evidence of the previous iridocyclitis was a few corneal deposits and the fine vitreous opacities.

The patient is now (1928) 17 years of age, and has remained well throughout the subsequent years.

ETIOLOGY

It is clear that our case corresponds with Heerfordt's description and belongs to the group of about forty cases which Berg [3] collected in a review of the literature up to 1924. Some of these cases may have represented atypical forms of mumps; others were regarded as tuberculous in origin; still others were viewed as syphilitic, while many were described as instances of Mikulicz's disease with ocular manifestations. Finally, a few ventured the opinion that uveoparotitis was caused by a specific virus, the nature of which was still to be discovered.

Heerfordt himself considered at great length the possible relation of this malady to epidemic parotitis, searching the literature thoroughly for examples of mumps with unusual ocular and nervous complications. A few reports of such cases were discovered, but, with the exception of two which undoubtedly belong to the disorder now under discussion, these unusual cases of mumps could be differentiated from subchronic uveoparotitis by the acuteness of their course which so obviously corresponded with that of an acute infectious disease that no doubt could be entertained concerning the etiology. Moreover, no secondary cases of mumps were traceable to Heerfordt's three patients, and when these patients were observed, the incidence of epidemic parotitis was low.

The question as to whether uveoparotitis subchronica originated from mumps was reopened when, in 1919, Weve [4] reported three cases similar to Heerfordt's as "Drei Fälle von Parotitis epidemica mit Iridozyklitis," basing his diagnosis of acute epidemic parotitis largely on the fact that one of the cases occurred during an epidemic of mumps, and that three secondary cases were apparently attributable to it.

The patient's illness which Weve described began with malaise, anorexia, fever and a lesion in the left eye, followed a month later by a transient right-sided facial palsy and a week later by a left-sided parotid swelling. About a month after the appearance of this enlargement, the right gland was similarly affected, and the right eye was cloudy. Another three months passed and the iridocyclitis in the left eye recurred. Improvement ensued in a month, and finally recovery was recorded about ten months after the onset of the illness.

Certainly this clinical picture is not that of mumps, and so the accuracy of Weve's caption of "Parotitis epidemica" may be seriously questioned.

3. Berg: Zentralbl. f. Ophth. **13**:254, 1924.
4. Weve: Arch. f. Augenh. **85**:203, 1919.

In the case of our own patient mumps could be practically excluded because the epidemic disease was not prevalent at the time of observation; no secondary cases could possibly have been attributed to him and besides, the boy had suffered a typical attacks of mumps two years before the illness for the relief of which we were consulted.

Following Weve's exposition of the mumps etiology of subchronic uveoparotitis, no further serious attention is given in the literature to such a possibility, and while not denying a specific virus for some cases of Heerfordt's disorder, the discussion has centered largely around the question whether tuberculosis or syphilis may be the causative agent, or whether uveoparotid fever should be classified as a variety of Mikulicz's symptom-complex. As a matter of fact, in a recent article on the latter syndrome, Schaffer and Jacobsen [5] have included febris uveoparotidea subchronica as one of its varieties. Nor are these authors the first to suggest this nosologic position, because in the previous year Reimers [6] concluded that Heerfordt's disease should be identified with one group of Mikulicz's syndrome, and almost at the same time Weve [7] used the hyphenated title "Mikulicz-Heerfordt" to describe several similar cases.

Assuming then for the present that febris uveoparotidea should be included in the broad scope of Mikulicz's syndrome, it follows that we are faced with many of the problems of etiology that have been encountered in analyzing the numerous examples of the disorder first described by Mikulicz.

It became evident long ago that Mikulicz's syndrome is not a pathologic entity but that it might occur under a variety of conditions or result from a number of causes.

In the article to which reference has been made, Schaffer and Jacobsen [5] have reviewed this syndrome from the standpoint of etiology, and it is interesting and suggestive to be able to duplicate in the published cases of Heerfordt's uveoparotitis many of the conditions and causes of the typical Mikulicz's symptom-complex which these authors describe. Thus, there is a familial form of Mikulicz's disease, and it should be recorded that in 1927 a familial form of uveoparotitis was reported by Weve [8] of Rotterdam. His two cases are significant not only because each of two brothers presented the same clinical picture at an interval of seven years at exactly the same age, but because an anatomic examination of the parotid tissue and of an affected lacrimal gland could be carried out in one of the cases. Later, reference will be made to these pathologic observations, but even with the histologic

5. Schaffer and Jacobsen: Mikulicz's Syndrome, Am. J. Dis. Child. **34**:327 (Sept.) 1927.

6. Reimers: Ztschr. f. Augenh. **60**:30, 1926.

7. Weve: Ztschr. f. Augenh. **60**:68, 1926.

8. Weve: Klin. Monatsbl. f. Augenh. **78**:83, 1927.

picture demonstrated and with other laboratory observations at hand, Weve had to conclude that he was dealing with a disorder of unknown origin.

The evidence that syphilis can produce Mikulicz's syndrome is not conclusive, although the incidence of syphilis in the reported cases is so high that the association seems more than fortuitous. Nevertheless, the undoubted etiologic rôle of syphilis cannot be established either in Mikulicz's syndrome or in subchronic uveoparotitis, although the spirochetic origin of the latter disorder has also been assumed. In Berg's [3] collected series of Heerfordt's syndrome there are only two cases in which parotid swelling and iridocyclitis were present with concomitant syphilis. Mohr's [9] case was the first to be described with this association, but there is little to be said in favor of the view that the positive Wassermann reaction in his patient was more than a coincidence.

While the leukemic process may initiate the development of Mikulicz's symptom-complex, especially in children, it does not play any part in the production of subchronic uveoparotitis. Whenever the blood has been examined in this condition, its cytology has been normal.

It has been proved, too, that lymphosarcoma may evoke Mikulicz's clinical picture but not the Heerfordt group of signs.

That tuberculosis plays its part in the causation of a group of Mikulicz's syndrome has undoubtedly been proved, and though a similar statement has been applied to Heerfordt's disease, it cannot be propounded with the same force because the tubercle bacillus has not been isolated in the latter variety as it has been in the classic type of Mikulicz's symptom-complex. It is certain that tuberculosis is not the sole etiologic agent of febris uveoparotidea as some of the German observers believe. It is only in some isolated instances that the strong probability of a tuberculous origin can be asserted. Thus, Kristine Lehmann [10] reported the subsequent history of one of the three cases which Heerfordt previously had published. Nodular lesions developed in the iris tissue; synechiae formed; vision diminished to finger counting; an iris bombée resulted, and iridectomy had to be performed. The piece of iris thus obtained revealed typical giant cells as well as epithelioid and round cells, but necrosis or tubercle bacilli were not discovered.

Gjessing,[11] too, has described an iridocyclitis in a girl, aged 11, with an accompanying bilateral parotid condition which, because of the phthisic appearance of the patient and a positive tuberculin reaction, he views as tuberculous and makes the deduction that Heerfordt's syndrome is only a peculiar reaction form of tuberculosis.

9. Mohr: Klin. Monatsbl. f. Augenh. **64**:694, 1920.
10. Lehmann, cited by Gjessing: Klin. Monatsbl. f. Augenh. **60**:249, 1918.
11. Gjessing: Klin. Monatsbl. f. Augenh. **60**:249, 1918.

In the most recent review of febris uveoparotidea and its relation to tuberculosis, Reimers [6] reports the case of a boy, aged 14, suffering from a parotitis chronica indurativa who four weeks later presented a bilateral iridocyclitis. Roentgenologic examination of the thorax revealed an enlargement of the hilum glands which was interpreted as being most probably due to tuberculosis of the bronchial glands. The iridocyclitis ran the course of a tuberculous nodular iritis. A piece of the parotid was excised and showed microscopically epithelioid tubercles. A tuberculin cure was promptly followed by an improvement. From these data and from a review of the literature, Reimers concludes rather cautiously that in the majority of cases of Heerfordt's disease, it is "fairly certain" that tuberculosis plays an etiologic rôle and that since in a series of cases of Mikulicz's syndrome tuberculosis undoubtedly is the causal agent, uveoparotitis should be identified with that group of Mikulicz's syndrome of tuberculous origin.

In this connection it should be noted that Weve's [8] observations on the two brothers previously quoted failed to furnish convincing evidence of the tuberculous origin of his "familial uveoparotitis," although the histologic examination of the parotid and lacrimal glands yielded the anatomic picture of epithelioid tuberculosis. Tubercle bacilli, however, could not be demonstrated. Furthermore, there was no family history of phthisis; a most careful and prolonged clinical observation failed to disclose the least suggestion of tuberculosis; the Pirquet reaction was always negative; injections of old tuberculin in a dose as high as 20 mg. did not give any reaction and inoculation of parotid and lacrimal gland tissue into the anterior chamber of rabbits and into the peritoneal cavity of guinea-pigs was attended with negative results. In view of these negative observations but taking into account the histology of the glands, Weve proposed that for the present the condition might be designated "paratuberculosis."

In the case of our patient diagnostic injections of tuberculin as high as 5 mg proved completely negative, and no sign of tuberculosis has developed during the five years that have elapsed since he was first seen.

From the foregoing, the confused state of opinion with regard to the possible tuberculous origin of uveoparotitis is disclosed. The confusion is not peculiar to the small group of uveal inflammations associated with subchronic parotitis. It extends to the subject of the relation of tuberculosis to ophthalmic lesions in general and is disclosed and considerably clarified in the recent publications of Kiefer and Shulman [12] in 1927, and of Wilmer [13] in 1928. As the tubercle bacillus has not been demonstrated in either the ocular tissues or the parotid glands of patients suffering from uveoparotitis, the criteria by which the tuber-

12. Kiefer and Shulman: Tr. Sect. Ophth., A. M. A., 1927.
13. Wilmer, W. H.: Arch. Ophth. **57:1**, 1928.

culous nature of some of these cases of uveoparotitis has been adjudged are the same as those employed in certain other groups of suspected tuberculous lesions of the eye unassociated with the Heerfordt-Mikulicz syndrome. The clinical ocular picture of uveoparotitis may be indistinguishable from the iridocyclitis tuberculosa as diagnosed by the expert ophthalmologist. Yet, the little iris nodule in uveoparotitis may have the yellowish-red hue suggestive of a syphilitic lesion, and so syphilis must be ruled out. Tuberculosis is assumed to be the causal factor when tuberculin in diagnostic doses evokes general, local and focal reactions either severally or in combination.

Gjessing's [11] patient, a girl, aged 11, with enlarged parotids, with numerous fine and coarse deposits on Descemet's membrane, hyperemic irides and synechiae received 1 mg. of old tuberculin and reacted with a temperature of 103.6 F., while the eyes reddened and the precipitates increased markedly.

Only a few such cases have been reported; the majority, like ours, have yielded negative results.

An obvious lesion in the lung or hilum glands is presumptive evidence that the uveoparotitis is tuberculous. Much stress is laid on the diagnostic value of an apparently successful tuberculin cure.

The last two factors together with the histologic observations in the parotid gland led Reimers [6] to conclude that tuberculosis was the basis of the changes in his case.

None of these standards alone can be accepted unreservedly in the positive diagnosis of the tuberculous nature of uveoparotitis, however, because the tuberculin reaction may be indicative of a tuberculous focus apart from that of the parotid glands, and this focus may be only a concomitant and not a causal factor; a tuberculin cure may be more apparent than real as some cases of uveoparotitis resolve spontaneously and not as the result of therapeutic efforts. On the other hand, the failure to demonstrate tubercle bacilli in the tissues either histologically or by inoculation does not exclude the tuberculous nature of the changes of the eye, since Finnoff [14] produced ocular tuberculosis in rabbits by the injection of dead tubercle bacilli into the common carotid artery.

Summing up the evidence, it may be said that the tuberculous origin of some cases of uveoparotitis cannot be denied, and this decision is reached because of the clinical appearance and course of the ocular lesions as evaluated by expert ophthalmologists; because of the microscopic structure of the lesions in the iris and parotid glands in the few cases in which this minute anatomic examination has been made and, finally, because of the importance attached to the diagnostic value and curative effects of tuberculin in the hands of competent observers.

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14. Finnoff: Tr. Am. Ophth. Soc. **21**:87, 1923.

SYMPTOMS AND SIGNS

It might be predicted *a priore* that the course of a condition without unity of etiology will vary, and so it is not surprising that there is not a definite order in the appearance of the chief symptoms and signs. The age incidence ranges from childhood to middle age. As a rule, there is a prodromal period characterized by the constitutional symptoms of an infection: malaise, anorexia and fever. The ocular lesion was the primary localization in our patient, but in others the parotid swelling has been the initial sign. Occasionally, the other salivary glands as well as the lacrimal are affected, and there may be a concurrent lymphatic glandular enlargement. The fever is usually not high, although at the onset of our patient's illness it registered 103 F. More often the temperature, while elevated, ranges from 99 to 101.5 F.

Paralysis of one or more of the cerebrospinal nerves is a complication which Heerfordt stressed. These paralyses have been repeatedly described and may modify the clinical picture considerably. The facial nerve is the most commonly involved, and the ensuing paralysis may be unilateral or bilateral. More rarely other nerves may be affected, so that Critchley and Phillips [15] in relating the clinical history of their patient feel justified in describing the syndrome as "iridocyclitis—parotitis—polyneuritis."

Besides the ocular lesion and the parotid swelling, the patient, a woman, aged 51 years, who had been ill two years, presented ptosis, facial asymmetry, the left nasolabial fold being more prominent, and distinct atrophy localized in the interossei and the muscles of the thumb. There was also some difficulty in swallowing.

One of Heerfordt's patients also had dysphagia, together with palatal and laryngeal paralysis and paresthesiae.

These neural complications commonly subside in a few weeks or months. Critchley and Phillips' case just cited forms an exception. The duration of the untreated parotid swelling is usually measured in months, but roentgenotherapy when instituted has a markedly beneficial effect leading promptly to its disappearance.

Unfortunately, it is the eye on which the brunt of permanent damage falls. Our patient recovered with only a few corneal deposits, and some fine vitreous opacities as evidence of the previous iritis, but usually the iridocyclitis is a relatively malignant process, bilateral, characterized by remissions and exacerbations. In most cases nodules form in the iris, and the collateral manifestations of uveitis—intra-ocular hypertension, keratitis, clouding of the lens and neuroretinitis are often present. Finally, the vision is frequently lost or almost abolished in at least one of the eyes.

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15. Critchley and Phillips: Lancet **207**:906, 1924.

TREATMENT

The probability of such a serious eventuality renders the attempt to combat the disorder a matter of great importance. If syphilis is demonstrated to exist in one of these patients, it is imperative that antisyphilitic treatment be instituted, even though its causal relation to the lesion is questionable. It is self-evident that the ocular condition must receive the continued care of a competent ophthalmologist, while the patient as a whole is treated in an attempt to increase what is vaguely understood as "resistance." In a more specific way this resistance can be raised when the etiologic probability of tuberculosis is great. Here tuberculin in proper hands is one of the most effective therapeutic agents. Reference has already been made to Reimers' case in which a tuberculin cure was promptly followed by a marked retrogression of the pathologic process. The use of tuberculin in the treatment of ocular lesions is discussed and illustrated in the recent papers of Kiefer and Shulman [12] and of Wilmer.[13]

Another valuable means of combating ocular tuberculosis as well as the totality of the uveoparotitic syndrome is radiotherapy. So far as the eye is concerned, Scheerer's [16] contribution in 1925 on "Roentgenbestrahlung bei Uveal Tuberkulose" is the most illuminating. Obviously, the collaboration of the experienced ophthalmologist and the expert roentgenologic therapeutist is an essential prerequisite. Under such conditions, Scheerer ventures the opinion that roentgen-ray radiation is undoubtedly a powerful measure in the treatment of patients with tuberculosis of the iris and that in no other way can the acute phenomena be so certainly and quickly dispersed. In early cases, the nodules on the iris disappear under radiation in a few days or weeks, leaving the tissues prepared for the further absorption of exudates.

Equally or perhaps more enthusiastically one can speak of the effect of radiation on the parotid tumors. As early as 1905,[17] the enlarged parotid and lacrimal glands characteristic of the typical Mikulicz's syndrome were successfully treated by the roentgen ray and radium, and ever since the literature has abounded in such reports, including as well cases of uveoparotitis.

The effect of three applications of radium to the swollen parotids of our patient was spectacular. Five days after the first treatment, the irradiated gland had diminished in size. Before radiation the enlarged salivary glands seriously impeded the boy's mastication. Within a month he was able to eat with ease and comfort.

In 1925, Byron H. Jackson [18] of Scranton reported a case of uveoparotitis in which the roentgen ray was applied to both parotid glands and the eyes with striking benefit.

16. Scheerer: Klin. Monatsbl. f. Augenh. **75**:27, 1925.
17. Van Duyse: Arch. d'ophth., December, 1905.
18. Jackson: Am. J. Ophth. **8**:361, 1925.

The patient was a woman, aged 27, whose illness had begun ten months previous to consulting Dr. Jackson in August, 1923. During this period, she had been treated for a condition characterized by enlargement of the parotid and lacrimal glands; bilateral iridocyclitis, a transient diplopia and a partial right-sided facial and parotid swelling persisted, and a cataract developed in the left eye. There had been a few lardaceous deposits on the posterior corneal surfaces, fine vitreous opacities in both eyes and numerous synechiae. "Six X-ray treatments were given one week apart as follows: 4 milliamperes, 125 kilovolts, 10 inch distance, five minutes, 5 mm. aluminum filter to each parotid and to each lacrimal gland, the eyes and surrounding tissue being protected from the rays." The glands decreased in size so rapidly that it was thought that the same treatment might terminate the accompanying iridocyclitis. "Therefore, five X-ray treatments at weekly intervals were given to each eye through the closed lids as follows: 4 milliamperes, 125 kilovolts, 10 inch distance, five minutes, 5 mm. aluminum filter." The improvement in the condition of the eyes began at once and continued, the inflammatory process coming to an end.

On the basis of his experience, Jackson makes a plea for early roentgenologic treatment in cases of uveoparotitis with the expectation of preventing the destructive sequelae of the ocular disorder.

SUMMARY

In summary, febris uveoparotidea subchronica should be regarded as a variety of Mikulicz's syndrome in which iridocyclitis is the outstanding and important concomitant. There is no unity of etiology. It has been described as a familial disorder; it may have a syphilitic origin; in some instances it is caused by tuberculosis, while in many as in the case of our patient the etiologic agent cannot be demonstrated.

Radiotherapy instituted promptly and expertly gives promise of terminating the pathologic process. Tuberculin similarly administered is a valuable adjuvant when tuberculosis is the probable cause.

THE USE OF DEXTROSE INTRAPERITONEALLY IN INFANTS AND IN YOUNG CHILDREN *

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For many years dextrose has been recognized as a carbohydrate which, when given orally or parenterally, is readily available for the purpose of combustion within the body. To give by mouth quantities sufficient to meet the needs of the special conditions for which this material is suited, and to give it in the dilution required to meet the needs of the organism is usually highly inconvenient or impossible, especially in infants and in young children. For the administration of dextrose subcutaneously, intravenously or intraperitoneally, an isotonic solution is, in most cases, desirable; this means a due consideration of the amounts to be used at any given time. This is especially true when the intravenous route is chosen because of the strain on the heart caused by large amounts of fluid introduced in this way, and when the subcutaneous route is used because of the mechanical restriction as to space and because of the pain due to stretching of the tissues.

In 1918, Blackfan and Maxcy [1] reported the use of physiologic sodium chloride solution intraperitoneally in seven cases of vomiting and diarrhea in infants. Though there is some probability that this procedure had been used for some time, the article by these authors is the first that we have been able to find on the subject. In 1919, Marriott [2] advocated the use of dextrose intraperitoneally in the treatment of athreptic infants. McLean and Lang,[3] in 1920, used a 6 per cent solution of dextrose intraperitoneally in young infants, and they do not mention alarming or even suggestive symptoms.

Mitchell,[4] in 1922, summing up the value of intraperitoneal injections in infancy, says of dextrose: "In the light of our present knowledge

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* From the Pediatric Department of Rush Medical College, the University of Chicago and the Children's Ward of the Presbyterian Hospital.

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1. Blackfan, K. D., and Maxcy, K. F.: Intraperitoneal Injection of Saline Solution, Am. J. Dis. Child. **15**:19 (Jan.) 1918.

2. Marriott, W. M.: Artificial Feeding of Athreptic Infants, J. A. M. A. **73**:1173 (Oct. 18) 1919.

3. McLean, S., and Lang, C. A.: Fluid Injections in Dehydrated Infants, Am. J. Dis. Child. **19**:359 (May) 1920.

4. Mitchell, A. G.: Arch. Pediat. **39**:291 (May) 1922.

it is better to introduce glucose or sodium bicarbonate intravenously if their use is so urgently indicated that the giving of these substances by mouth will not suffice."

Evidently the use of dextrose had not been without untoward results. In 1921, Maches [5] had already reported cases in which rise in temperature, cyanosis and weak pulse had followed the injection of dextrose into the peritoneal cavity; this experience was confirmed by Gittings and Donnelly,[6] and Crawford [7] mentioned abdominal distention. Tenzer and Ebel [8] consider its use as an heroic measure.

Soria and Halac,[9] while advocating the use of isotonic dextrose solution intraperitoneally in cases of bronchopneumonia, always kept a solution of 1:1,000 epinephrine on hand to combat shock following the administration of dextrose.

The experience noted in these reports is that of all who have used dextrose intraperitoneally, so that it was felt generally that some remedy must be found or the useful procedure abandoned. In 1922, Williams and Swett [10] found that solutions of dextrose rapidly become acid on autoclaving and that the toxic action is due to this acidity. For reducing acidity, they advised buffering the solution. Solutions so buffered were used intravenously with success by Stoddard.[11] It occurred to us that the prevention of this acidity would be as effectual as its neutralization and somewhat simpler, and with that in mind we decided to determine if this could be done by sterilizing the dextrose in a perfectly dry state and by making the solution immediately before use, especially since buffering the solution had not proved entirely successful in all instances.

Our first experiments with solutions of dextrose were carried out on dogs. Solutions of dextrose, after boiling for twenty minutes or autoclaving, were allowed to stand at laboratory temperature. These were injected intraperitoneally at various lengths of time. The resulting reactions increased in intensity with the length of time following sterilization. Three hours after sterilization of the solution of dextrose, reactions would develop following injection. These varied from simple distention to severe shock when specimens that had stood a longer time were used.

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5. Maches, S.: München. med. Wchnschr. **68**:1082 (Aug. 26) 1921.

6. Gittings, J. C., and Donnelly, J. D.: Intraperitoneal Injections of Salt Solution, Am. J. Dis. Child. **23**:124 (Feb.) 1922.

7. Crawford: Illinois M. J. **47**:374 (May) 1925.

8. Tenzer and Ebel: Monatschr. f. Kinderh. **33**:295 (March) 1926.

9. Soria, B., and Halac, E.: Rev. méd. cubana **38**:369 (April) 1927.

10. Williams, J. R., and Swett, Madeline: Hydrogen ion Concentration Studies on Distilled Water, Physiologic Sodium Chloride, Glucose and Other Solutions Used for Intravenous Medication, J. A. M. A. **78**:1024 (April 8) 1922.

11. Stoddard, J. L.: Boston M. & S. J. **191**:1121 (Dec.) 1924.

Buffering the solution was successful in a majority of cases, but as in a few cases nausea developed, it was decided to overcome the tendency to acid formation in another way. This was done by autoclaving the dextrose dry and then by adding sterilized water to it. There were no effects of any kind in the dogs injected intraperitoneally with the solution in this manner.

METHOD

Chemically pure dextrose is used. Five grams are accurately weighed and placed in a pyrex tube measuring 150 by 200 mm. These tubes must be thoroughly dried by a hot blast and by baking for forty minutes at 100 C. The tube is now plugged by a piece of gauze 20 by 20 cm., and four thicknesses are used. A sterile "four" makes an ideal plug. This gauze is placed over the top of the tube and pushed down into the bore for about 10 cm. A small piece of cotton is placed at the bottom of the cartridge formed, and about 5 Gm. of porous calcium chloride is poured above this. The gauze is now twisted well into the tube, leaving enough at the top to extract it easily.

These tubes are now autoclaved at 15 pounds (6.8 Kg.) of pressure for twenty minutes and are ready for use. These will keep for at least fourteen days, which is the longest time that we have ever allowed them to stand.

Tubes that show any brown spots in the dextrose or moisture in the plug should not be used.

One hundred cubic centimeters of double distilled water is added to the dextrose when ready for use, and a 5 per cent solution is thus obtained. It is our custom to mark each tube at its capacity of 100 cc. and to pour the water directly into the tube. It was found that a higher concentration than 5 per cent tended to draw body fluid into the abdominal cavity, which corresponded to the observations of Narat.[12] Obviously, this would be undesirable in a dehydrated child.

The usual sterile procedure and point of injection into the abdomen[13] is used.

Table 1 shows our experience with this method of treatment in infants and young children.

An analysis of the "deaths" is necessary if we are to obtain a proper estimate of the results obtained (table 2).

The one death occurring in intoxication occurred in a child admitted in a moribund state, to whom three injections of 100 cc. were given. Death in this instance was not prevented, but it was not caused by the procedure. In the other cases of this condition as many as six injections in twenty-four hours were given with definitely beneficial results. In one instance marked distention occurred, and injections were discontinued.

One of the four deaths occurring in cases of bronchopneumonia was that of an infant suffering from purulent bronchopneumonia complicated by congenital heart disease to whom two injections were given.

12. Narat, A. K.: Ann. Surg. **78**:357, 1925.

13. Sanford, H. N.: Treatment with Intraperitoneal Injection of Neoarsphenamine, J. A. M. A. **85**:242 (July 25) 1925.

In two instances the injections were given for intoxication (eighteen and six injections, respectively) from which the infants recovered. Each developed (five and three weeks afterward) bronchopneumonia when the injections (four and two, respectively) were repeated, but death intervened. No untoward reactions which we could attribute to dextrose were seen in either case.

TABLE 1.—*Results of Intraperitoneal Injections of Dextrose Into Infants and Young Children*

Diseases	Cases	Total Injections	Deaths
Severe dehydrating diarrhea	25	250	1
Decomposition	3	18	..
Lobar pneumonia	8	24	..
Bronchopneumonia	14	56	4
Pyelitis	6	22	..
Tonsillitis	14	42	..
Postoperative: 3 intussusception, 1 peritonitis	4	12	1
Syphilis: dextrose, neoarsphenamine	2	8	1
Total	76	432	7

TABLE 2.—*Deaths After Injections of Dextrose*

Disease	Number	Injections	Comment
Severe dehydrating diarrhea	1	3	Admitted moribund; 3 injections given
Bronchopneumonia	1	2	Purulent bronchopneumonia; congenital heart disease
	2	30	Both cases originally intoxicated; had 18 and 6 injections and recovered; both developed bronchopneumonia just before discharge and died after 4 and 2 injections each
	1	12	Secondary to pertussis; 4 injections daily for three days
Syphilis	1	2	Florid syphilis; 50 injections of neoarsphenamine given in dextrose; immense reaction, rise in temperature to 105 F., vomiting and cyanosis; collapse; repeated in four days, same reaction; died in eighteen hours; no autopsy; patient in similar case given 4 injections of dextrose and neoarsphenamine; had no reactions and negative Wassermann reaction in four weeks
Postoperative intussusception	1	2	Not brought to hospital until forty-eight hours after diagnosis; moribund; one injection given at operation, second three hours after; child died two hours after operation, typically toxic

The fourth death occurred in a case of bronchopneumonia secondary to pertussis, four injections of dextrose were given daily for three days. The diagnosis was confirmed at autopsy. Peritoneal reactions were not noted.

In the cases of congenital syphilis death occurred in a case of florid syphilis. The child had a definite reaction to dextrose when first given intraperitoneally 50 mg. of neoarsphenamine in 100 cc. of 5 per cent dextrose; the temperature rose to 105 F.; the patient vomited, became cyanosed and collapsed. Neoarsphenamine when given in the usual dilution without dextrose did not produce any reaction, but a second

injection of neoarsphenamine in dextrose solution was followed by death in eighteen hours. Unfortunately, autopsy was not allowed. In a second case in which the patient was similarly treated with a complete series of injections of neoarsphenamine in 5 per cent dextrose solution a reaction did not occur and the Wassermann test was negative in four weeks.

The case of intoxication in which distention occurred and the case of congenital syphilis in which the patient died both occurred during the same period. It happened at this time that we were unable to obtain the brand of dextrose that we had used before and have used since, and that the calcium chloride used in the cartridge was powdered rather than granular. Whether or not these conditions may explain the untoward results we do not know, but in view of our uniformly good results, except in these two instances, we feel that these circumstances deserve consideration.

The other death occurred in a case of intussusception in which the patient was not brought to the hospital until forty-eight hours after the beginning of symptoms. One injection was given at the time of operation and a second three hours thereafter. The child died seven hours after operation.

From our experience here noted, we feel that 5 per cent dextrose solution given intraperitoneally may prove a valuable therapeutic measure in a variety of conditions provided that the dextrose is sterilized in the dry state and the solution made up immediately before using.

We also feel that this method of preparation if properly and carefully carried out insures against shock following the administration of dextrose.

FACTORS INFLUENCING THE EXCRETION OF CALCIUM *

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The amount of calcium excreted in the stools of a normal breast-fed infant is quite a large part of the calcium ingested. It is a remarkable fact that even breast-fed infants rarely absorb as much as 50 per cent of the calcium in the milk while, with the exception of magnesium, only a small part of the other mineral substances generally remains unabsorbed. In a paper dealing with the calcium and phosphorus metabolism of premature infants, published by one of us (B. H.) several years ago,[1] the argument was put forward that the large part of the ingested calcium which reappears in the stools must have some function to fill in the body. After discussing the various possibilities, the conclusion was arrived at that the calcium in the stools probably originates chiefly from calcium excreted into the intestine after having played a rôle in the acid-base metabolism of the body.

The question whether the calcium in the stools represents unabsorbed calcium, the function of which (whatever it may be) has been restricted to the intestinal tract, or calcium, absorbed and reexcreted into the colon after having filled some function in the internal metabolism, has not yet been answered in a satisfactory manner. There seems to be no doubt that under special conditions calcium may be excreted into the gastro-intestinal tract, at least in animals. It has been shown, for instance, that after the administration of parathyroid extract-collip to dogs, there may be an increase of the excretion of calcium in the stools.[2] In human subjects, however, the increase in the excretion of calcium on the administration of parathyroid extract-collip takes place entirely through the kidneys.[3] After intravenous injection of calcium chloride in dogs, an increase of the excretion of calcium in the stools has been found.[4] Ross and Scriver [5] reported that an increase in the calcium in

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* From the Children's Division of the Massachusetts General Hospital and the Department of Pediatrics, Harvard Medical School.

1. Hamilton: Acta Paediat. **2**:1, 1922.
2. Greenwald and Gross: J. Biol. Chem. **66**:217, 1925.
3. Albright (personal communication).
4. Greenwald and Gross: J. Biol. Chem. **66**:201, 1925.
5. Ross and Scriver: Proceedings American Pediatric Society, 1926, Am. J. Dis. Child. **32**:637 (Oct.) 1926.

the stool occasionally occurs after the administration of ammonium chloride to infants, and Shohl and Sato [6] made the same observation when an infant was given hydrochloric acid. In all these instances, however, there is no way of knowing whether the increased excretion of calcium in the stools is the result of increased calcium content of all glandular secretions into the gastro-intestinal tract, from the saliva downward, or whether the excretion has taken place in some restricted part of the intestine as a specific function of that part. Bergeim [7] has published a preliminary communication of experiments on rats which seem to show that calcium is absorbed in the upper part of the small intestine and reexcreted into the colon.

The most exhaustive study of the excretion of calcium in infants has been published by Telfer,[8] who is of the opinion that in infants there is no evidence of reexcretion of calcium into the colon. He bases this opinion, it seems, on the parallelism between the calcium intake and the fecal excretion of calcium, and also on the fact that calcium is excreted chiefly as insoluble tertiary phosphates. Although these facts make it seem rather probable that the calcium in the stools has never left the gastro-intestinal tract, they are, perhaps, not altogether inconsistent with the theory that the colon serves as an organ of excretion for calcium.

The purpose of the experiments now to be reported was to investigate the relationship between the excretion of calcium in the stools and the intake of mineral substances in the milk. It seemed to us that the question of the excretion of calcium should first be studied in infants nourished with breast milk. Infants fed on cow's milk formulas generally receive from two to six times as much calcium, depending on the formula, as breast-fed infants of the same age. This large excess of calcium intake may possibly obscure the fundamental laws of calcium metabolism, and as cow's milk also in many other respects constitutes an abnormal food, it is conceivable that adjustments are taking place in the metabolism, making the picture less clear. It seemed possible that the best understanding of calcium metabolism might be obtained by the study of those variations in the excretion of calcium which are often found in normal infants fed on breast milk. If the cause of these normal variations could be understood, we might, perhaps, be better equipped to study the calcium metabolism under abnormal conditions. Our plan was to keep an infant under ideal conditions as far as possible, to feed it on breast milk and to study the variations in the excretion of calcium which we hoped would occur.

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6. Shohl and Sato: J. Biol. Chem. **58**:257, 1923.
7. Bergeim: Proc. Soc. Exper. Biol. & Med. **23**:777, 1925-1926.
8. Telfer: Quart. J. Med. **16**:45 and 63, 1922; **17**:245, 1923; **20**:1 and 7, 1926.

A premature infant was studied since such an infant is especially well suited for this kind of study. If fed on breast milk and protected from infections, premature infants generally grow rapidly, which makes it seem probable that they utilize the food as well as circumstances allow, thus reducing to a minimum the danger of overfeeding and lack of utilization from that cause. During the course of the study, the infant developed the usual early craniotabes of premature infants, but otherwise did not show any abnormal symptoms. Early craniotabes in premature infants should probably not be regarded as true rickets, as it generally is not accompanied by a low blood phosphorus.[9]

The infant was studied during fifteen periods, mostly of six days' duration. Eleven of these periods will be reported here; seven were "normal" periods in which nothing but breast milk[10] was given; four were special periods in which some additions were made to the breast milk.

METHOD

The infant was kept on the Gamble metabolism bed. Stools and urine were collected, the few grams of food which the infant would spit up, occasionally were weighed, and an aliquot sample was taken each day from the breast milk from which the infant had been fed the previous day. The stools were dried on the water bath, homogenized by stirring them with ether until the ether had evaporated, heated for a few minutes at 100 C., and weighed. The urine was preserved with toluol, the milk with thymol.

The calcium and total fixed base in the stool and the milk was determined in solutions of the ashed material (ashed according to Stolte[11]), the calcium in the urine was precipitated direct in the urine, and the total fixed base in the urine was determined after digestion with acid in the usual way. The method of Fiske was used for determining calcium[12] and total fixed base.[13] Chloride was determined direct in the stool, milk and urine, by the method of Fiske and Lin.[14] For the determination of phosphorus, the method of Fiske and Subbarow[15] was used. The inorganic phosphorus in the urine was determined direct in the urine. Total phosphorus in stool and milk was determined in specimens ashed by the Stolte method after the addition of sodium carbonate, and then dissolved in the molybdate solution used in the foregoing method (Molybdate I). Inorganic phosphorus in the milk was determined in the following manner suggested by Dr. Fiske: To 4 cc. of breast milk is added 1 cc. of 40 per cent trichloracetic acid. The precipitate is filtered off, and 2 cc. of the filtrate (which is not quite clear), is neutralized with dilute ammonia in a 50 cc. centrifuge tube, using phenolphthalein as an indicator. Six drops of a saturated solution of lead acetate are then added, and the fluid mixed and centrifugalized. After the supernatant fluid has been

9. Sisson: Proceedings American Pediatric Society, 1927, Am. J. Dis Child. **34**:302 (Aug.) 1927.
10. The milk was pooled breast milk from five to ten women.
11. Stolte: Biochem. Ztschr. **35**:104, 1911.
12. See Hamilton, J. Biol. Chem. **65**:101, 1925.
13. Fiske: J. Biol. Chem. **51**:55, 1922.
14. See Fiske and Sokhey: J. Biol. Chem. **63**:310, 1925.
15. Fiske and Subbarow: J. Biol. Chem. **66**:375, 1925.

carefully poured off, the residue is dissolved in 2.5 cc. of Molybdate I, according to the Fiske-Subbarow method, and transferred to a test tube graduated at 25 cc. The determination is then continued in the usual way.

Potassium was determined by the Fiske method (not yet published). Magnesium was precipitated as pyrophosphate (after the removal of calcium) and

TABLE 1.—*Experimental Periods of Case B. S., Values Calculated for One Day*

Period	Date	Days	Weight, Gm.	Gain, Gm.	Milk, Cc.	Urine, Cc.	Dry Stool, Gm.	Stool Water, Gm.	Comments
					"Normal" Periods				
I	11/29–12/ 4	6	3,070	17	601	381	4.270	....	
II	12/ 7–12/ 9	2	3,350	..	719	470	6.988	....	
IV	12/15–12/21	6	3,600	45	716	470	4.555	....	
V	12/30– 1/ 5	6	4,105	33	735	479	3.713	16.3	
VI	1/ 7– 1/13	6	4,235	18	727	453	3.189	14.0	
VII	1/15– 1/20	5	4,360	25	743	453	3.155	14.5	
X	2/24– 3/ 2	6	5,080	14	771	457	2.755	17.9	
					"Special" Periods				
VIII	1/24– 1/30	6	4,600	18	740	481	4.089	11.0	0.5 Gm. of sodium bicarbonate daily
XI	3/ 9– 3/18	9	5,220	8	794	479	3.094	10.3	1 Gm. of sodium citrate daily
XIIa	3/24– 3/29	5	5,530	24	874	563	2.537	11.1	64 cc. tenth-normal hydrochloric acid daily
VIIb	3/29– 4/ 3	5	5,530	24	875	545	3.073	11.0	63 cc. tenth-normal hydrochloric acid daily
XIII	4/ 8– 4/14	6	5,855	5	869	476	3.513	13.9	2 Gm. of sodium bicarbonate daily

TABLE 2.—*Calcium Metabolism: Values in Cubic Centimeters Tenth-Normal Calcium Daily*

Period	Intake	Urine	Stool	Total Output	Absorption*	Retention	Comments
				"Normal" Periods			
I	86	4	64	68	22	18	
II	86	5	69	74	17	12	
IV	106	4	56	60	50	46	
V	95	5	52	57	43	38	
VI	99	4	52	56	47	43	
VII	94	6	51	57	43	37	
X	119	4	64	68	55	51	
				"Special" Periods			
VIII	91	5	72	77	19	14	0.5 Gm. sodium bicarbonate
XI	130	7	85	92	45	38	1 Gm. sodium citrate
XIIa	132	11	56	67	76	65	64 cc. tenth-normal hydrochloric acid
XIIb	125	10	69	79	56	46	63 cc. tenth-normal hydrochloric acid
XIII	122	8	69	77	53	45	2 Gm. sodium bicarbonate

* By "absorption" is meant that part of the intake which does not reappear in the stools (calcium intake minus stool calcium).

the phosphorus content of the precipitate determined by the Fiske-Subbarow method. The values for sodium were obtained by subtracting potassium, calcium and magnesium from the total fixed base.

Some general data in regard to the eleven periods in which the infant was studied are found in table 1. Table 2 shows the calcium metabolism.

TABLE 3.—*Intake of Milk, Nitrogen and Inorganic Substances in Tenth-Normal Phosphorus Taken as Trivalent, Values Calculated for One Day*

Period	Milk, Cc.	Nitrogen, Gm.	Phosphorus, Cc.			Chlorine, Cc.	Calcium, Cc.	Magnesium, Cc.	Potassium, Cc.	Sodium, Cc.	Total Base, Cc.
			Total	Organic	Inorganic						
I	601	1.23	121	63	58	74	86	14	97	91	288
II	719	1.26	87	46	41	83	86	6?	82	149	323
IV	716	1.37	81	31	50	75	106	17	79	49	251
V	735	1.10	96	46	50	76	95	19	80	59	253
VI	727	1.14	117	73	44	73	99	14	74	51	238
VII	743	1.27	82	30	52	72	94	19	79	53	247
X	771	1.32	89	39	50	76	119	21	89	32	261

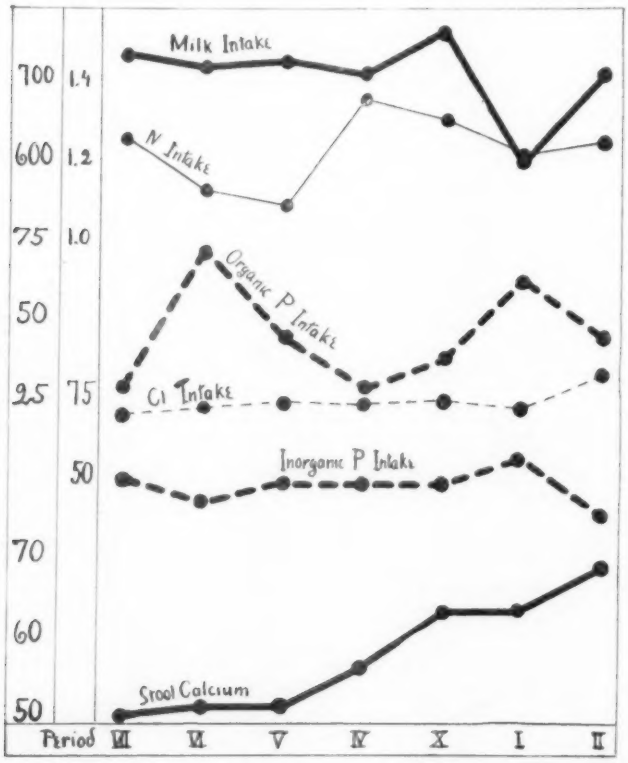

Fig. 1.—The excretion of Ca in the stools compared with the amounts of milk taken and with the intake of N, P and Cl. (For easy comparison the various curves in this chart and in figure 2 are drawn at different levels and to different scales, indicated by the figures on the left; see tables 1 and 3.)

In charts 1 and 2, the excretion of calcium in the stools has been compared with the amount of milk given to the infant, with the intake of nitrogen and with the intake of various mineral substances. Each dot on the curves represents a value obtained in one experimental period. The periods are ranged, not in the order in which they occurred, but according to the amount of calcium in the stools. The bottom curve,

representing variations in the calcium in the stools, shows, consequently, a steady rise from left to right in the diagram, and all curves begin with period VII in which the amount of calcium in the stools was lowest.

Chart 1 shows that there was no parallelism between the amount of milk given to the infant and the excretion of calcium in the stools; nor could any relationship be found between the intake of nitrogen, phosphorus and chlorine and the excretion of calcium. Of interest

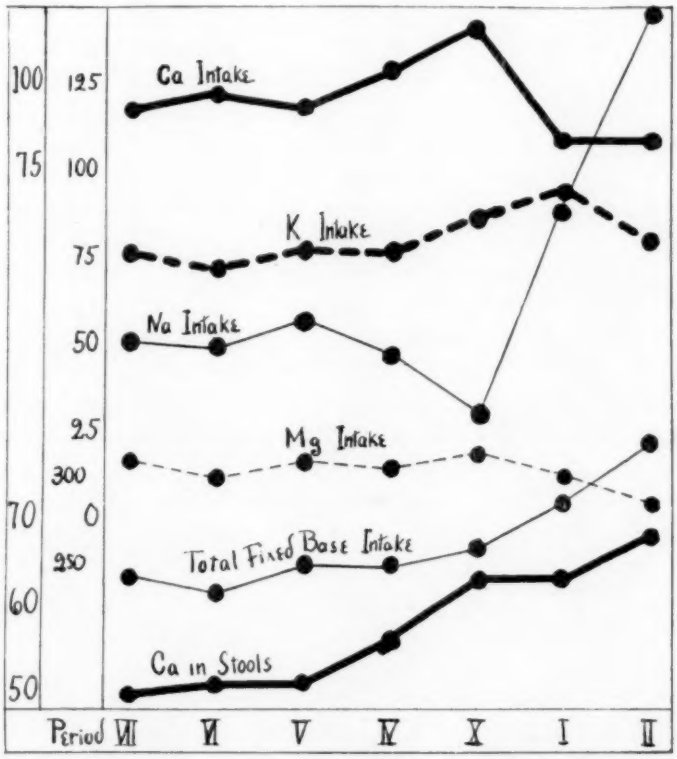

Fig. 2.—The excretion of Ca in the stools compared with the intake of Ca, K, Na, Mg and total fixed base. (For easy comparison the various curves in this chart and in figure 1 are drawn at different levels and to different scales, indicated by the figures on the left; see tables 1 and 3.)

is the fact that the nitrogen and the organic phosphorus in the milk nearly always show variations in opposite directions.

Chart 2 shows that there is little relationship between the excretion of calcium and the intake of the various milk bases (calcium, magnesium, potassium and sodium). Certain parts of the curves for calcium, potassium and sodium show some degree of parallelism with the curve

for excretion of calcium in the stools, but if all periods are considered, no definite relationship can be found. It is interesting to note that the sodium and calcium in the milk nearly always show variations in opposite directions.

Chart 2 shows further that although the individual bases do not show any relationship to the excretion of calcium, such a relationship seems to exist between the total intake of fixed base and the excretion of calcium.

Consequently, to judge from these diagrams, it seems that of the various factors investigated, the intake of total fixed base is the only one that shows any relationship to the excretion of calcium in the stools. The relationship between graphic curves, however, is always difficult to evaluate, especially when curves are made up of a comparatively small number of observations. In order to be sure that the interpretation which we have given to the diagrams is correct, we have calculated the correlation coefficients between the calcium in the stools on one side and the milk bases, separate as well as the total base, on the other side. (A correlation coefficient of plus or minus 1 indicates perfect correlation; a coefficient of 0 indicates that no correlation exists between the two variables. The standard error of the coefficient has, however, also to be taken into account, and conclusions cannot be drawn unless the coefficient is at least three times as large as its standard error.)

The result of these calculations was as follows: The correlation coefficient between the calcium in the stools and the fixed base intake is $+0.91 \pm 0.07$; between the calcium in the stools and the calcium intake is, -0.07 ± 0.38; between the calcium in the stools and the magnesium intake, -0.55 ± 0.26; between the calcium in the stools and the potassium intake, $+0.65 \pm 0.22$, and between the calcium in the stools and the sodium intake, $+0.69 \pm 0.20$.

These correlation coefficients show that our interpretation of the diagrams was correct. The total fixed base is the only one of these factors which shows a definite relationship to the excretion of calcium in the stools. This relationship may also be studied by means of the regression equation. If there were a perfect mathematical relationship between fixed base intake and excretion of calcium in the stools, then it should be possible to calculate the one from the other. The regression equation shows the degree of accuracy with which this can be done. The regression equation in this case is : $X_1 = 0.22\,X_2 + 0.6$, where X_1 is the calcium in the stool, X_2 the fixed base intake. If the calcium in the stool is calculated from the fixed base intake by means of this equation, the result shown in table 4 is obtained.

In all but one period, the calcium in the stools may be calculated from the fixed base intake with a fair degree of accuracy, but in this one period (X) the disagreement is so marked that we must conclude that some other factor in addition to the fixed base intake has also influenced the excretion of calcium in the stools. This factor must have influenced the excretion of calcium but little in all the other periods. It need not, necessarily, have been a factor connected with the food of the infant. On looking over the various curves in the diagrams, it is striking that in period X the curve for calcium intake shows a high peak, and this fact makes it seem probable that it is the high calcium intake in this period which has influenced the excretion of calcium and caused the disagreement between the actual amount of calcium excreted and the calculated amount. In order to find out whether this was true, the correlation has been calculated between the

TABLE 4.—*Calcium in the Stools Calculated from Fixed Base Intake*

Period	Actual Amount, Ce.	Calculated Amount, Ce.	Difference, per Cent of Actual Amount
VII	51	54	— 6
VI	52	52	0
V	52	55	— 6
IV	56	55	+ 2
X	64	57	+11
I	64	62	+ 3
II	69	71	— 3

three variables: calcium in the stools, calcium intake and fixed base intake. The regression equation between these three factors is: $X_1 = 0.32\,X_2 + 0.31\,X_3 - 55$, X_1 being calcium in the stools; X_2, calcium intake, and X_3, intake of total fixed base. Table 5 shows with what degree of accuracy the calcium in the stools may be calculated from this equation.[16]

It is evident that by means of this equation the calcium in the stools may be calculated from the calcium intake and the fixed base intake with great accuracy. The differences between the actual and the calculated values are so small that they fall within the limits of error set by the methods employed. If still other factors have influenced the excretion of calcium in the stools, they must either have varied in exactly the same manner as the two factors found, or their influence has been very small.

16. The equations given here have, of course, no general validity. They present, in mathematical terms, a picture of the relationships existing in this infant at the time the study was made.

We know, however, that there are such factors. It has been shown that an excessive intake of fat [17] or of phosphorus [18] may increase the amount of calcium in the stools. It may be concluded from our experiments that if the normal variations in the fat and in the phosphorus content of the breast milk have any influence on the excretion of calcium, this influence must be small.

Calcium is excreted in the stools chiefly as tertiary phosphate and as soaps. The formation of these compounds is dependent on the reaction, and a change of the reaction in the direction of alkalinity will make the conditions more favorable for the formation of calcium soaps and tertiary calcium phosphate. It has already been shown that the excretion of calcium in the stools is directly parallel to the intake of fixed base and the probable explanation of this fact is the influence which the base must have on the p_H of the intestinal content. In 100 cc. of breast milk there is about 40 cc. tenth-normal fixed base. Only

TABLE 5.—*Calcium in the Stools Calculated from Calcium Intake and Fixed Base Intake*

Period	Actual Amount, Cc.	Calculated Amount, Cc.	Difference, per Cent of Actual Amount
VII	51	51	0
VI	52	51	+2
V	52	54	—4
IV	56	56	0
X	64	64	0
I	64	61	+5
II	69	72	—4

about 10 cc. tenth-normal of this is bound as chloride, the rest of the base is bound chiefly as phosphate and to weak acids (organic acids, carbonic acid and protein), and this part of the base represents the buffer value of the milk. This part of the base (base minus chloride), in our experiments, was in a constant relationship to the total base (correlation coefficient $+0.999 \pm 0.0004$), and the variations of the total base were, therefore, an indicator of the variations in the buffer content of the milk. The p_H in the upper part of the small intestine must be dependent chiefly on three factors: (1) the amount of acid secreted into the stomach, (2) the amount of alkali secreted into the intestine and (3) the buffer value of the food. When, as in our experiments, only longer periods are taken into account (generally six days), the two first mentioned factors will probably vary but little

17. Lindberg: Ztschr. f. Kinderh. **16**:90, 1917.

18. Orr, Holt, Wilkins and Boone: Relation of Calcium and Phosphorus in Diet to Absorption of These Elements from Intestine, Am. J. Dis. Child. **28**:574 (Nov.) 1924.

from period to period, and variations of the third factor will then result in parallel variations of the intestinal p_H.

If it is true that the small normal variations in the buffer content of the milk have an influence on the excretion of calcium in the stools, it need not, necessarily, follow that more marked variations, such as may be obtained by the administration of acid or alkali, would have the same effect. The constancy of the gastric and intestinal secretions is a *sine qua non,* without which no parallelism between milk buffer and calcium in the stools may be expected. Any marked variations in the composition of the food will, however, in all probability result in changes in the gastro-intestinal secretions. For instance, Hoffmann and Rosenbaum,[19] using the sugar-curve method, found that the amount of gastric juice secreted by an infant is proportionate to the protein content of the milk, and Babbott and his co-workers [20] found an increased hydrochloric acid secretion when the amount of milk was increased. It would, therefore, probably be a mistake to assume that if, for instance, alkali is added to the milk, this alkali would be the only new factor in the acid-base situation in the gastro-intestinal tract. The conditions probably would be complicated by changes in the gastro-intestinal secretions, and whatever change might take place in the intestinal p_H would be the result not only of the administration of alkali, but of a chain of events impossible to follow by quantitative determinations. It is, therefore, not to be wondered at that the published reports on the effect of the administration of acid or alkali on the excretion of calcium in the stools are rather contradictory. Flood,[21] in experiments with artificially fed infants, found that when a rachitic infant was given hydrochloric acid milk, the excretion of calcium in the stools was decreased. With normal infants, however, this effect was not obtained. Shohl and Sato,[6] on the other hand, found increased excretion of calcium on the administration of 250 cc. of tenth-normal hydrochloric acid daily, and the same result was obtained on administration of alkali (473 cc. tenth-normal sodium bicarbonate daily).

We have made some experiments with the infant here studied in which alkali and acid was added to the breast milk. As both the intake of fixed base and the intake of calcium have an influence on the excretion of calcium in the stools, each experimental period should be compared with a control period, having about the same intake of fixed base and calcium as would have been furnished by the milk

19. Hoffmann and Rosenbaum: Jahrb. f. Kinderh. **96**:164, 1921.

20. Babbott, Johnston, Haskins and Shohl: Hydrogen Ion Concentration of Gastric Contents, Am. J. Dis. Child. **26**:475 (Nov.) 1923.

21. Flood: Calcium Balance with Hydrochloric Acid Milk, Am. J. Dis. Child. **32**:550 (Oct.) 1926.

given in the experimental period without its addition. This was impossible, as the breast milk varied a great deal in its composition. The equation given on page 457, however, gives a good picture of the extent to which changes in fixed base intake and calcium intake influenced the excretion of calcium in the normal periods, and it seems probable that if acid or alkali had not been given, these two factors would have influenced the excretion of calcium in about the same way at the time when the acid and alkali experiments were undertaken. In the normal periods, the excretion of calcium in the stools could be calculated from the equation with an accuracy of 5 per cent or less. A marked disagreement between the calcium in the stools actually found in the acid and alkali experiments and the calcium in the stools calculated from the milk without its addition would probably be due to the addition of alkali or acid to the milk. No conclusions may be drawn, of course, unless the disagreement is marked. A disagreement of 20 per cent or

TABLE 6.—*Calcium in the Stools Found During Acid and Alkali Experiments*

Period	Actual Amount, Cc. N/10	Calculated Amount,* Cc. N/10	Difference, per Cent of Actual Amount
VIII, 59 cc. tenth-normal sodium bicarbonate	72	36	+50
XI. 98 cc. tenth-normal sodium citrate	85	81	+ 5
XIII, 239 cc. tenth-normal sodium bicarbonate	69	82	—19
XIIa, 64 cc. tenth-normal hydrochloric acid	56	87	—55
XIIb, 63 cc. tenth-normal hydrochloric acid	69	85	—23

* These values are calculated by means of the equation from the values for calcium intake (table 2) and the following values for milk base: VIII, 214; XI, 214; XIIa, 324; XIIb, 323; XIII, 332. The value in period VIII is obtained by subtracting 59 cc. (0.5 Gm. of sodium bicarbonate) from the amount of base which the infant received. The values in periods XI and XIII were obtained by actual determinations in samples of milk taken before the addition of the alkali.

more has been interpreted as a positive result. The result of the experiments are shown in table 6.

When a small dose of alkali was given (VIII), the amount of calcium excreted in the stools was considerably more than the expected value. A dose twice as large did not seem to have any effect on the excretion of calcium (XI). The largest dose (XIII) resulted in a somewhat lower value of calcium in the stools than was expected, but the difference between the calculated value and the amount of calcium actually found in the stools in this period was hardly marked enough to allow any definite conclusions.

Period XII, in which acid was added to the milk, was divided into two parts of five days each, immediately following each other. This division was made in order to find out whether the immediate effect of the administration of acid might be more marked than later when acid had been given for some time. This was found to be the case. The excretion of calcium in period XIIa was decidedly lower than the expected value, while in period XIIb the difference was much less

marked. It would have been interesting to see whether on still more prolonged administration of acid the effect would have entirely disappeared.

The comparison of the values for the excretion of calcium in these periods with values calculated from the equation is, of course, open to criticism. The equation gives a picture of the relationship between calcium in the stools, calcium intake and base intake in the normal periods, in which the values for calcium in the stools varied between 51 and 69 cc. of tenth-normal calcium daily. If, in the alkali and acid periods, the calculated values would have fallen within this range, there would have been hardly any objection to the use of the equation. Unfortunately, however, owing to variations in the intake of calcium and of base, the calculated values were either below or above the range of the stool calcium in the "normal" periods; it might be argued that the validity of the equation for values outside this range has not been proved. This is true, but the equation would probably have to be changed only a little to cover values outside the range, as it had reference to the same infant at practically the same time. By not considering any differences between the actual values and the calculated values, that were less than 20 per cent of the former, we have probably safeguarded ourselves against any error that the use of the equation might involve.

Consequently, the result of these experiments was that when the calcium in the stools in the experiments with acid and alkali was compared with the expected values for calcium in the stools (calculated from the equation) a small dose of alkali seemed to increase and a small dose of acid to decrease the excretion of calcium in the stools. The doses of acid and alkali which had this effect did not change the buffer content of the milk beyond the limits of variations in the "normal" periods. When larger doses of alkali were given, the results were indefinite. The normal variations here reveal a relationship which is less clearly apparent under artificial experimental conditions.

The influence which the milk base has on the calcium in the stools probably proves that the latter was formed before the former was absorbed, that is, in the small intestine. The other alternative, that some kind of antagonism exists between calcium and other base in the internal metabolism, seems much less probable.

The parallelism between the total fixed base in the milk and the buffer content of the milk, together with the result of the acid and alkali experiments, makes it seem probable that the important factor in relation to excretion of calcium is not the intake of total fixed base, but the intake of buffer (base minus chloride). If this is true, then the factors in the food which would influence the excretion of calcium in the stools would be: the buffer content, the calcium content, the phosphorus content and the fat content, the two last mentioned having

an influence on the excretion of calcium only when ingested in excessive amounts. Other factors which possibly might influence the excretion of calcium suggest themselves: secretion of hydrochloric acid into the stomach, the secretion of the pancreas, the liver and the intestinal mucosa. Experiments are now being planned with the purpose of investigating some of these factors.

CONCLUSIONS

1. The normal variations of the excretion of calcium in the stools of a breast-fed infant were studied; it was found that the excretion of calcium was influenced chiefly by the intake of total fixed base, to a lesser degree by the intake of calcium. As the total fixed base was closely related to the buffer content of the milk (base minus chloride), it seems probable that it was the buffer content of the milk which had this influence on the excretion of calcium in the stools. This view is strengthened by the results in some experiments in which acid and alkali were added to the milk.

2. The close relationship between calcium in the stools and milk base makes it probable that the former was formed before the latter was absorbed, that is, in the small intestine.

TREATMENT OF FUSOSPIRILLARY INFECTIONS OF THE MOUTH IN CHILDREN

WITH SPECIAL REFERENCE TO THE INTRAMUSCULAR ADMINISTRATION OF SULPHARSPHENAMINE *

HAROLD K. FABER, M.D.
SAN FRANCISCO

The reported success of many local agents of widely differing chemical composition in the treatment of fusospirillary infections of the mouth, such as ulcerative gingivitis and ulcerative tonsillitis, may be explained, in part at least, as being due to the effectiveness of simple removal of debris and perhaps also to the promotion of local nonspecific tissue and leukocyte stimulation. The long list of such local agents includes hydrogen peroxide, potassium chlorate, chromic acid, methylene blue, silver nitrate, various combinations of ipecac or emetin with arsenic and glycerin, and solutions or suspensions of one or another of the arsphenamine series. The most recent addition to the list is sodium perborate, advocated in the form of a paste by Bloodgood.[1]

While doubtless the condition in a majority of cases will sooner or later yield to local chemical treatment and in some cases to simple thorough local cleansing, in a considerable number it almost interminably resists such therapy, nor is it an easy matter in the individual case to state in advance whether or not local treatment is going to be effective. It is well to remember that in a certain though small percentage of cases, the disease advances more or less rapidly to serious stages and may even threaten life. Furthermore, in children, local treatment is effectively applied with the greatest difficulty, and in the youngest children local treatment is almost impossible. On the whole, the difficulties and uncertainties of local treatment in young children are sufficiently marked to afford clear grounds for preferring the systemic approach, provided that the latter is effective. Children under 6 or 7 years of age could hardly be expected, for instance, to give satisfactory cooperation with Bloodgood's method, which requires the perborate paste to be held five minutes in the mouth.

My own unsatisfying experience with various local methods of treatment of Plaut-Vincent infections of the mouth, particularly ulcera-

* Received for publication, May 26, 1928.

* From the Department of Pediatrics, Stanford University Medical School, San Francisco.

1. Bloodgood, J. C.: Oral Lesions Due to Vincent's Angina: What Every Physician and Dentist Should Know About Its Recognition and Treatment, J. A. M. A. **88**:1142 (April 9) 1927.

tive gingivitis, has led me to employ, as a matter of routine, the intramuscular administration of sulpharsphenamine. In one or two earlier cases, neoarsphenamine was used. The effectiveness of arsphenamine therapy in fusospirillary infection was demonstrated in 1910 by Ehrlich [2] in a case reported in detail by Gerber.[3] In the same year, Gerber [3] showed by a careful study that after the administration of arsphenamine the spirochetes in actual lesions of the mouth lost their motility within twenty-four hours and disappeared shortly, while those on normal mucous surfaces were unaffected. In 1910 also, Rumpel [4] reported seven cases of fusospirillary infection of the mouth in which the patients were successfully treated with arsphenamine. Ehrlich's patient was well in four days. In Rumpel's series, recovery was complete in from six to sixteen days. Various favorable reports have appeared since that time, among which may be mentioned those of Sebenq,[5] Pereira,[6] Davis and Pilot,[7] Barenberg and Bloomberg [8] and Mikell.[9] Barenberg and Bloomberg reported a series of cases in twenty-six children between the ages of 22 months and 4 years who were treated by sulpharsphenamine given intramuscularly; and in about one half of the cases, the treatment was given locally. The results were almost uniformly good, in spite of the small doses (0.1 Gm.) used in a majority of the cases.

The present report is therefore not of a new or untried procedure, but rather of one which appears to have been undeservedly neglected. Holt and Howland, for example, do not mention it in the last edition of their book. The reasons for the neglect of this procedure are not wholly clear, but the following may be suggested: 1. The visible improvement is preceded by a period of from one to four days during which the lesions may not be visibly improved. Gerber [3] has shown that actual improvement is going on during this latent period. 2. When too small doses are given (as in some of Barenberg and Bloomberg's cases),

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2. Ehrlich, P.: (Discussion) München. med. Wchnschr. **57**:2268 (Oct. 25) 1910.

3. Gerber: Weitere Mitteilungen über die Spirochäten der Mundrachenhöhle und ihr Verhalten zu Ehrlich-Hatas 606 (Salvarsan), Deutsche med. Wchnschr. **36**:2383 (Dec. 22) 1910.

4. Rumpel, T.: Unsere bisherige Erfahrungen mit dem Ehrlichschen Präparat 606, Deutsche med. Wchnschr. **36**:2286 (Dec. 8) 1910.

5. Sebenq, C.: L'angine de Vincent, Thèse de Paris, 1919, no. 139.

6. Pereira, A. M.: L'angine de Vincent à marche extensive et son traitement par l'injection intraveineuse de neosalvarsan, Thèse de Paris, 1921, no. 432.

7. Davis, D. J., and Pilot, I.: Studies of Bacillus Fusiformis and Vincent's Spirochete, J. A. M. A. **79**:944 (Sept. 16) 1922.

8. Barenberg, L. H., and Bloomberg, M. W.: The Use of Sulpharsphenamin in Vincent's Angina and Stomatitis in Children, J. A. M. A. **83**:25 (July 5) 1924.

9. Mikell, P. V.: Vincent's Angina, Ann. Otol. Rhin. & Laryng. **35**:528 (June) 1926.

the therapeutic effect may be incomplete or unduly delayed. 3. A considerable proportion of patients is cared for by dentists who are professionally limited to local methods of treatment. 4. The disease is often considered by physicians to be a mild one, to be handled in the office rather than in the hospital, and therefore preferably by local means. 5. The supposed difficulties of administration of arsphenamines in small children are often deterrent.

The introduction of sulpharsphenamine with its relative ease of administration has lessened such difficulties. The drug can be given in full doses with little discomfort and with satisfactory therapeutic results. I have given doses calculated from age and body weight as I do in the treatment of patients with syphilis. With one or two exceptions, only one dose has been given. In the following series, one or two cases are included in which the patients were treated with neoarsphenamine, but for the last two years sulpharsphenamine alone has been employed.

REPORT OF CASES

CASE 1.—A girl, aged 26 months, was admitted to the clinic on Nov. 23, 1925, with the history of a sore mouth and fever of one week's duration. The gums were swollen, red and bled easily and presented many shallow ulcers. The tonsils showed a grayish, slimy exudate. The temperature was normal. The smears on this day were negative for spirilla and fusiform bacilli. Local treatment with 1 per cent gentian violet was given for two days. On November 25, smears were positive and 0.2 Gm. of sulpharsphenamine was given intramuscularly. Local applications of emetin and solution of potassium arsenite were also begun at this time. Two days later visible improvement in the mouth was striking. On November 30, the mouth was clear. The child was last seen in the clinic on Feb. 1, 1927, at which time the mouth was normal. The condition had not recurred.

CASE 2.—A girl, aged 2, was admitted to the clinic on Nov. 30, 1925, with a history of sore mouth, fever and loss of appetite for nine days. The gums were red and bled easily. There was a whitish ulcer on the left tonsil, and considerable cervical adenitis. The temperature was normal. Smears from the tonsillar ulcer showed fusiform bacilli and spirilla. Sulpharsphenamine (0.2 Gm.) was given intramuscularly on November 30. No other treatment was given excepting a mouth wash of a weak solution of sodium bicarbonate. On December 2, the tonsillar ulcer was smaller but the gums remained red and swollen. The next day the child was dismissed as the ulcer was practically healed and the gums much better. When seen two and a half months later, the child's mouth appeared normal, and there had been no recurrence of ulcers or inflammation of the gums. At this time a cervical gland had become swollen and softened and required incision. This was done at another hospital, and no trace of the patient could be found after April, 1928.

CASE 3.—A girl, aged 22 months, was first seen by me on May 6, 1926, because of ulcers on the tongue and gums which bled easily. She was treated in the clinic with local applications of 1 per cent gentian violet for four days without improvement, and was admitted to the hospital where, on May 11, the smears taken showed spindles and spirals. Sulpharsphenamine (0.1 Gm.) was given intramuscularly on May 12. No other treatment was employed. The next day the mouth appeared clean excepting that the gums were slightly swollen and bled

easily. She was dismissed and was next seen in the clinic six days later, at which time the mouth was found to be normal. There were no further visits to the clinic and the family could not be traced.

CASE 4.—A girl, aged 19 months, was admitted to the clinic on Oct. 10, 1926, with a small grayish ulcer on the left tonsil and a temperature of from 103 to 104 F. On October 13, ulcers on the tip of tongue were also noted. Smears showed Plaut-Vincent organisms. Sulpharsphenamine (0.2 Gm.) was given intramuscularly October 14, and a mouth wash was prescribed (kind not specified in the notes). On October 16, the mouth was "practically cleared up," but (for some reason which is not clear) another dose of 0.2 Gm. of sulpharsphenamine was given. On October 19, the mouth appeared normal, and the child was dismissed as cured the next day. There was no return visit, and the family could not be traced.

CASE 5.—A girl, aged 3, was admitted to the clinic on Nov. 20, 1926, with a history of swollen, red, easily bleeding gums showing shallow ulcers. The patient was treated with emetin and solution of potassium arsenite for two days. She showed slight subjective improvement but the condition of the gums remained unchanged; there were also shallow ulcers on the tongue and lips. There was no fever at this time. Smears were positive. Sulpharsphenamine (0.2 Gm.) was given on November 22. No other treatment was applied. By November 24, the lesions were "considerably cleared up," and the patient was dismissed. When visited at home, April 10, 1928 (sixteen and one half months later), the patient's mouth was found to be normal, and there had been no recurrene of the condition.

CASE 6.—A boy, aged 2, was brought to the clinic because of crusts on the lips, ulcers on the buccal membrane and the tongue; swollen gums that bled easily when touched and marked cervical adenopathy. The mouth had been sore for one week. A single smear was negative for Plaut-Vincent organisms, but clinically the case closely resembled a fusospirillary infection. Local treatment with emetin and solution of potassium arsenite was begun on Feb. 7, 1927. On February 8, 0.1 Gm. of sulpharsphenamine was given intramuscularly; twenty-four hours later, the stomatitis was "75% improved." By February 12, the condition was practically cured. The patient did not return to the clinic and could not be traced.

CASE 7.—A girl, aged 13, was admitted to the clinic with the history of several attacks of gingivitis, diagnosed as Vincent's infection by her dentist. She was treated with emetin and solution of potassium arsenite applied locally three times daily; in spite of this, there was a recurrence five weeks later. The smear showed many spirilla and fusiform bacilli. Sulpharsphenamine (0.4 Gm.) was given intramuscularly on Dec. 17, 1927. On December 21, the mouth was much improved, but the gums were still slightly congested and showed a whitish marginal deposit. A second dose of 0.5 Gm. was given. She was next seen on Jan. 7, 1928, at which time the mouth was clear, and the smear was negative for spirals and spindles. On April 18, the mouth was clear, and there had been no recurrence.

CASE 8.—A boy, aged 2, was brought to the clinic on Dec. 16, 1927, because of severe gingivitis with many spirals and spindles in the smear. One treatment with 2 per cent gentian violet was given, and a mouth wash of hydrogen peroxide was prescribed. On December 20, the condition of the mouth was much worse. Neoarsphenamine (0.3 Gm.) was given intramuscularly and emetin and solution of potassium arsenite prescribed for local treatment. Three days later, the mouth was greatly improved. From that time improvement was gradual, and a normal

appearance of the gums was not noted until January 11. On April 10, the mouth appeared normal and there had been no recurrence.

CASE 9.—A boy, aged 15 months, was admitted to the clinic on Jan. 3, 1928, with marginal ulcers of the gums and a few small ulcers on the tongue. The temperature by rectum was 39 C. (102 F.). The first smears were negative. Many spindles and spirals were found in smears from the ulcers on January 6. Sulpharsphenamine (0.2 Gm.) was given intramuscularly on January 7. A 3 per cent solution perborate mouth wash was used after feedings. On January 8, there was some improvement. By January 10, the temperature was normal; the visible improvement was striking. The next day the ulcers appeared to be completely healed and the mouth normal. When visiting the patient at his home three months later, the mouth was found to be normal; there had been no recurrence of the condition.

CASE 10.—A girl, aged 2, was presented at the clinic with the history of fever, excessive salivation, ulcers on the mucous membranes of the lips, tongue and upper poles of the tonsils and an edematous pharynx, which symptoms had been present for three days. The temperature was 38.6 C. (101.8 F.) by rectum. Smears showed many spindles and spirals. A dose of 0.2 Gm. of sulpharsphenamine was given on Jan. 28, 1928. A mouth wash of 1 per cent sodium perborate was given after feedings. On January 30, the appearance of the mouth and pharynx was greatly improved, and the temperature was 37.6 C. (99.6 F.). On the following day, the temperature was normal; the mouth was further improved, but the gums still bled easily. Another injection of 0.2 Gm. of sulpharsphenamine was given on January 31 (this appears not to have been entirely necessary), and the mouth wash of perborate was discontinued. On February 2, the mouth appeared practically normal and the child was dismissed from the hospital. On examination in the clinic two weeks later the gums were found to be slightly reddened and receding and the teeth dirty, but there were no ulcers and no other lesions of the mucous membrane. On April 11, there had been no return of sores on the gums, tongue, cheeks or throat, and the gums were not bleeding. The teeth were still carious and dirty.

CASE 11.—On admitting a boy, aged 10, to the clinic on Feb. 20, 1928, for another complaint, the gums were found to be slightly inflamed. Twenty-four hours later they were much inflamed and showed marked marginal ulceration. Marked cervical adenitis was present. The temperature was 39.6 C. (103.2 F.) by rectum. Smears showed many spirals and fusiform bacilli. Sulpharsphenamine (0.45 Gm.) was given intramuscularly on February 21. Eighteen hours later, the temperature was lower and the mouth less sore, but the appearance of the gums was unchanged. Other treatment was not given. On February 23, the soreness had nearly disappeared, and the gums looked slightly less inflamed. On February 24, the temperature was normal, the gums only slightly hyperemic, and the ulcers nearly healed. The cervical adenitis was less marked. On February 26, the boy was dismissed, apparently cured. On April 24, the mouth was normal and there had been no recurrence.

CASE 12.—A boy, aged 8, was admitted to the hospital for removal of tonsils and adenoids. Moderate inflammation of the gums with small marginal ulcers was noted. The temperature was 37.8 C. (100 F.) by rectum. Smears were positive for Plaut-Vincent organisms. A dose of 0.35 Gm. of sulpharsphenamine was given intramuscularly on Feb. 24, 1928. No other treatment was employed. The temperature was normal on the following day. On February 26, the gums appeared practically normal. Six weeks later, the mouth was normal, and there had been no recurrence of the condition.

COMMENT

The results have been reasonably uniform. It will be noted that in cases 3, 5, 7 and 8, local treatment had previously been tried without effecting a cure. Marked visible improvement occurred during the first twenty-four hours in two cases; in two days, in six cases; in three days, in three cases, and in four days, in one case. Complete restitution of visible integrity of the gums required considerably longer in most cases, but there was no failure in the series which comprises all those patients treated by my associates and me in the last two years. In several instances, there was an interval of several days between the time of dismissal from hospital and the next inspection in the clinic. Apparent healing had occurred in one case in two days; in two cases, in four days, in four cases, in five days and in one case, in seven days. In the rest the data are incomplete. Two children were dismissed much improved on the third and fourth days, respectively, and were not heard from again. One child was not seen between the fourth and twenty-second days and returned with the mouth normal. In one patient (8) treated by neoarsphenamine intravenously, improvement was definitely slow and was not complete until the twenty-first day. In the nine cases with follow-up records there had been no recurrences; one was followed for six weeks after treatment; six, for periods of from two to three and a half months; two, for fourteen and sixteen months, respectively. While the series is small, the uniform absence of recurrences is striking and stands in contrast to the results of other forms of treatment. Thus, Griffith and Mitchell[10] stated: "Even the milder cases occasionally become somewhat chronic in spite of treatment. Relapses are prone to occur."

The dosage now employed is approximately 15 mg. of sulpharsphenamine per kilogram of body weight. In some of the earlier cases, smaller doses were followed by the prompt recovery of the patient, but I believe that a single full dose is necessary to give assurance of the maximum therapeutic effect. When the intramuscular route is employed, there appears to be no serious objection to administration of the drug in the office, provided that the course of the disease can be reasonably well followed thereafter. I do not believe local administration of arsphenamine to be necessary or advantageous, since with full intramuscular doses the beneficial effects appear to be obtained with maximum rapidity Thus, in the present series the effects were noted in a considerably shorter time than in Barenberg and Bloomberg's series, in which smaller intramuscular doses were used in conjunction with local administration. It is, I believe, rarely necessary to give a second dose. I have done so more than once, but in reviewing the case records I am inclined to think

10. Griffith, J. P. C., and Mitchell, A. G.: The Diseases of Infants and Children, ed. 2, Philadelphia, W. B. Saunders Company, vol. 2, p. 13.

that I was too impatient of results. Often the lesions appear unchanged after one or even two days and will suddenly, on the third or fourth day, appear almost healed. In some instances the temperature is a better guide than the local appearances, and drops to normal within one to two days. Simple mouth washes or applications, such as weak solutions of hydrogen peroxide, sodium bicarbonate or sodium perborate, are useful to cleanse the mouth, and particularly the ulcers, of debris. Parents and nurses, however, should be warned not to attempt vigorous cleansing of the lesions, which are readily traumatized by such measures.

CONCLUSIONS

1. The therapeutic effect of parenteral administration of members of the arsphenamine series in the treatment of fusospirillary infections of the mouth, particularly of ulcerative gingivitis, appears to be specific and marked.

2. For various reasons which have been discussed, this method of treatment has decisive advantages over local methods particularly in small children.

3. The intramuscular injection of sulpharsphenamine is advocated.

4. A single full dose of approximately 15 mg. for each kilogram of body weight is, in most cases, adequate to effect marked visible improvement in from one to four days.

5. Emphasis is laid on the frequent occurrence of a latent period of from one to three days after treatment during which visible improvement may not be noted. During this period, however, subjective improvement may occur and the temperature may drop to normal.

6. Local treatment may be used as an auxiliary measure, but need consist only of simple cleansing solutions applied gently.

THE RESPIRATORY METABOLISM IN INFANCY AND IN CHILDHOOD

IX. THE RESPIRATORY EXCHANGE IN MARASMUS: CARBOHYDRATE METABOLISM OF NORMAL AND OF MARASMIC INFANTS WITH AND WITHOUT THE ADMINISTRATION OF INSULIN *

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The fact that marasmic infants fail to gain weight in spite of large diets and in the absence of parenteral infection or alimentary disturbance suggested the possibility that some derangement of the intermediary metabolism might play a rôle in producing marasmus or maintaining it when once established. This paper deals with one phase of intermediary metabolism; namely, the effect of dextrose both with and without the administration of insulin on normal and marasmic infants.

The view has been frequently expressed that the metabolism of carbohydrate is abnormal in marasmus. Evidence for and against this theory has been recently and extensively reviewed by Tisdall.[1] Data obtained from studies of the respiratory exchange are, however, not available. In the present communication, the attempt has been made to throw some light on this question.

In the preceding paper, the basal metabolism in marasmus [2] was considered. Other phases will be dealt with in subsequent communications.

METHODS

Descriptions of the technical procedures, the metabolism ward,[3] the apparatus and the calculation of results [4] were published in earlier communications.

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1. Tisdall, F. F.; Drake, T. G. H., and Brown, A.: The Carbohydrate Metabolism of the Marantic Infant, Am. J. Dis. Child. **30**:829 (Dec.) 1925.

2. Levine, S. Z.; Wilson, J. R., and Gottschall, G.: The Respiratory Metabolism in Infancy and in Childhood: VIII. The Respiratory Exchange in Marasmus: Basal Metabolism, Am. J. Dis. Child. **35**:615 (April) 1928.

3. Wilson, J. R.; Levine, S. Z., and Rivkin, H.: The Respiratory Metabolism in Infancy and in Childhood: II. Ketosis and the Respiratory Exchange in Children Am. J. Dis. Child. **31**:335 (March) 1926.

4. Levine, S. Z., and Wilson, J. R.: The Respiratory Metabolism in Infancy and in Childhood: I. Basal Metabolism of Children, Am. J. Dis. Child. **31**: 323 (March) 1926.

The reliability of the apparatus was controlled by frequent alcohol checks, a detailed report of which was presented in previous papers (checks for the year ending July, 1926, in paper VI [5] and for the year ending July, 1927, in paper VII [5]).

During the year ending July, 1926, the respiratory quotients secured from alcohol, which are used as a means of calculating the foodstuffs oxidized, averaged 0.673, with maximum variations from 0.67 to 0.69 for individual determinations as compared with the theoretic quotient of 0.667. For the year ending July, 1927, the respiratory quotients for alcohol averaged 0.670 with maximum variations from 0.66 to 0.68 for individual determinations (paper VII [5]).

Two groups of patients were studied. The first group included three healthy infants, ranging in age from 2¼ to 7¼ months. The second group included three marasmic infants ranging in age from 2¾ to 9¾ months. One of the latter infants (A.S.) was studied both while in a state of severe malnutrition and about three months later, after he had gained in both weight and stature. In the latter instance, he was considered normal. His subsequent growth and development, as observed in the outpatient department, seemed to confirm this opinion. All of the patients were free from demonstrable evidences of parenteral infection or of alimentary disturbances during the entire period of observation in the metabolism ward. In the intervals between observations in the respiration chamber, all patients received adequate diets. The urines did not contain sugar.

All subjects [6] were given large feedings of dextrose dissolved in water before they were placed in the respiration chamber. The amount administered was previously calculated to be about the caloric equivalent, in dextrose, of one third of the total twenty-four hourly basal caloric requirement. Observations were made after these meals without and with the previous subcutaneous injection of insulin. The composition of meals and the time of administration in the experiments with insulin are recorded in table 1.

Immediately after receiving the dextrose meal, the patients were placed in the respiration chamber. The first measurements were recorded after the subject fell asleep and experimental conditions were satisfactory. The intervals between the ingestion of food and the beginning of the first period averaged fifty-eight minutes (table 1). Each experiment

5. Levine, S. Z.; Wilson, J. R; Berliner, F., and Rivkin, H.: The Respiratory Metabolism in Infancy and in Childhood: VI. The Specific Dynamic Action of Food in Normal Infants, Am. J. Dis. Child. **33**:722 (May) 1927. Levine, S. Z., and Wilson, J. R.: The Respiratory Metabolism in Infancy and in Childhood. VII. Elimination of Water Through the Skin and Respiratory Passages of Infants, Am. J. Dis. Child. **35**:54 (Jan.) 1928.

6. An exception to this statement will be found in the case of J. B., who received diluted whole milk, dextrimaltose and farina (table 1, column 7).

TABLE 1.—*Calorimeter Data in Terms of Averages Per Hour*

Case	Name	Experiment No.	Date	Weight, Kg.	Surface Area, Sq. M.*	Time	(1) Carbon Dioxide, Gm.	(2) Oxygen, Gm.	(3) Respiratory Quotient	(4) Urinary Nitrogen, Gm.	(5) Urine Sugar (Total), Gm.	(6) Average Rectal Temperature, F.	(7) Comment†
								Control Infants					
1	J. B.	3	1/22/26	6.11	0.34	11:19 a.m. to 12:51 p.m.	6.06	4.71	0.94	0.067	0.0	98.5	Milk, 110 cc.; dextrimaltose, 7.5 Gm.; farina, 5.0 Gm.; water, 57.0 cc.; calories, 135.9; 10:00 to 10:08 a. m.
		7	2/ 1/26	6.22	0.34	11:30 a.m. to 1:30 p.m.	5.71	4.39	0.95	0.057	0.0	98.8	Same meal as above; 10:16 to 10:21 a. m.
2	C. H.	17	4/16/26	5.67	0.32	2:49 p.m. to 4:49 p.m.	5.48	3.97	1.00	§	0.0	98.6	Dextrose, 22.0 Gm.; water, 180.0 cc.; calories, 81.4; 2:02 to 2:15 p. m.
		18	4/19/26	5.68	0.32	11:15 a.m. to 1:18 p.m.	5.58	4.09	0.99	0.069	0.0	98.8	Dextrose, 35 Gm.; water, 180 cc.; calories, 129.5; 10:20 to 10.25 a. m.
		24‡	5/ 3/26	5.78	0.32	11:43 a.m. to 1:43 p.m.	5.70	4.27	0.97	0.046	0.0	98.5	Dextrose, 27 Gm.; water, 136 cc.; calories, 99.9; 10:40 to 10:55 a. m. Insulin, 15 units at 10:30 a. m.
		25‡	5/14/26	6.01	0.33	12:20 p.m. to 2:20 p.m.	5.82	4.30	0.99	0.061	0.0	99.0	Dextrose, 35 Gm.; water, 90 cc.; calories, 129.0; 11:08 to 11:24 a. m. Insulin, 10 units at 10:57 a. m.
5	A. S.	54	1/19/27	6.24	0.34	11:06 a.m. to 1:21 p.m.	7.52	5.08	1.08	0.091	0.0	99.3	Dextrose, 45 Gm.; water, 240 cc.; calories, 166.5; 10:13 to 10.25 a. m.
		55‡	1/21/27	6.28	0.34	11:03 a.m. to 12:18 p.m.	7.32	5.27	1.01	0.082	0.0	100.0	Dextrose, 45 Gm.; water, 240 cc.; calories, 166.5; 9:59 to 10:07 a. m. Insulin, 11.5 units at 9:39 a. m.
								Marasmic Infants					
5	A. S.	28	10/22/26	3.47	0.23	11:00 a.m. to 1:15 p.m.	4.96	3.71	0.97	0.046	0.032	98.6	Dextrose, 35 Gm.; water, 140 cc.; calories, 129.5; 10:00 to 10:09 a. m.
		29‡	10/25/26	3.64	0.24	11:10 a.m. to 12:40 p.m.	5.31	3.72	1.04	§	0.0	99.0	Dextrose, 35 Gm.; water, 140 cc.; calories, 129.5; 10:06 to 10:15 a. m. Insulin, 10 units at 9:51 a. m.
		39	11/19/26	4.23	0.26	11:12 a.m. to 1:42 p.m.	5.21	3.89	0.98	0.041	0.0	98.9	Dextrose, 35 Gm.; water, 140 cc.; calories, 129.5; 10:27 to 10:39 a. m.
8	C. F.	48	12/29/26	4.76	0.28	11:19 a.m. to 12:34 p.m.	6.14	4.76	0.94	¶	0.36	98.9	Dextrose, 35 Gm.; water, 160 cc.; calories, 129.5; 10:31 to 10:37 a. m.
		50	1/ 3/27	4.76	0.28	11:00 a.m. to 1:00 p.m.	6.90	4.84	1.04	0.093	0.84	99.3	Dextrose, 35 Gm.; water, 160 cc.; calories, 129.5; 10:00 to 10:22 a. m.
		49‡	12/31/26	4.76	0.28	11:10 a.m. to 1:10 p.m.	6.48	4.52	1.04	0.081	0.0	98.1	Dextrose, 35 Gm.; water, 160 cc.; calories, 129.5; 10:23 to 10:27 a.m. Insulin, 10 units at 10:08 a. m.
10	V. O'B.	63	2/21/27	2.75	0.20	11:00 a.m. to 1:30 p.m.	3.38	2.44	1.01	0.039	0.206	96.6	Dextrose, 18 Gm.; water, 105 cc.; calories, 66.6; 10:17 to 10:19 a. m.
		65‡	2/23/27	2.78	0.20	11:05 a.m. to 1:45 p.m.	3.74	2.61	1.04	0.037	0.185	99.2	Dextrose, 18 Gm.; water, 105 cc.; calories, 66.6; 10:15 to 10:19 a. m. Insulin, 5 units at 10:08 a. m.

* Derived from figures of Benedict and Talbot (Carnegie Inst. of Wash., no. 302, 1921, table 15, p. 62).
† Patients slept throughout.
‡ Designates experiments in which insulin was administered.
§ Part of urine specimen lost. The remaining specimen did not show sugar.
¶ Urinary nitrogen not recorded because of loss of specimen following determination of sugar.

was divided into two or more periods of from three-fourths to one and one-half hours. This procedure served as a check on the reliability of observations and made possible the termination of experiments before the patients awoke by discarding final periods whenever necessary. Patients were studied, therefore, only during sleep.

Blood samples were taken before the ingestion of dextrose and again after the infant was removed from the respiration chamber and were analyzed for sugar [7] and carbon dioxide.[8]

The urine was collected as described in a previous communication. The time of the last voiding before the ingestion of dextrose and of the first voiding following removal from the chamber were carefully recorded. The total nitrogen and sugar content were determined.

HISTORIES OF CASES

CASE 5.—A. S., a white boy, born June 13, 1926, was admitted to the hospital at the age of 7 weeks with severe diarrhea. The past and family histories were unimportant. His weight at birth was 6 pounds 11 ounces (3,039.3 Gm.). On admission, he weighed 6 pounds (2,727.5 Gm.). The diarrhea persisted for about three weeks, during which time the patient also suffered from bilateral otitis media. Convalesence was interrupted by an attack of bronchopneumonia followed by extensive furunculosis. The boy recovered, however, and passed through a protracted convalescence during which time the gain in weight was extremely slow. On Oct. 15, 1926, when transferred to the metabolism ward he presented the picture of severe marasmus. At that time he was 4 months old and weighed 7 pounds 5 ounces (3,373.5 Gm.). During the period of study he was afebrile and did not show evidences of infectious processes.

After a short period in the metabolism ward, the patient began to gain. The weight curve rose steadily and fairly rapidly. He was again studied when his weight much more nearly approached normal and when he appeared in every other respect to be normal. His weight at the time of each experiment is recorded in table 3, column 1. Additional evidence supporting the opinion that the infant was in a healthy condition when studied the second time is the fact that he was reported well and weighing 21 pounds (9,525 Gm.) at the age of 1 year. The Wassermann and tuberculin tests were negative.

CASE 8.—C. F., a colored boy, born March 5, 1926, entered the hospital on December 3 of the same year because of mild diarrhea and malnutrition. He weighed 9 pounds 5 ounces (4,224 Gm.). The past and family histories were unobtainable, the patient being a foundling. The diarrhea disappeared in a few days. From December 13 to 17, the patient had an elevation of temperature associated with an infection of the upper respiratory tract. Recovery was uneventful. During the period that followed, the patient was studied in the metabolism ward. At this time he was afebrile and did not show any evidence of infection. On December 21, when admitted to the metabolism ward, he was

7. Folin, O., and Wu, H.: A System of Blood Analysis: Supplement I. A Simplified and Improved Method for Determination of Sugar, J. Biol. Chem. **41**: 367 (March) 1920. Rothberg, V. E., and Evans, F. A.: A Modified Folin and Wu Blood Sugar Method, J. Biol. Chem. **58**:443 (Dec.) 1923.

8. Van Slyke, D. D., and Stadie, W. C.: The Determination of the Gases of the Blood, J. Biol. Chem. **49**:1 (Nov.) 1921.

9½ months old and weighed 10 pounds 5 ounces (4,677.6 Gm.). His weight during experimental periods is recorded in table 3, column 1. The Wassermann and tuberculin tests were negative.

CASE 10.—V. O'B., a white girl, born Nov. 27, 1926, was admitted to the hospital on Dec. 30, 1926, because of vomiting and failure to thrive. On admission, the weight was 5 pounds 8 ounces (2,494.7 Gm.). Both parents were well. The patient was the youngest of seventeen children, six of whom are now living. She was born at term after an uneventful labor. Her weight at birth was 5 pounds (2,267.9 Gm.). During the first month she received breast milk and supplementary feedings of cow's milk. She did not thrive and gained only a few ounces. Refusal of food and vomiting began at about two weeks after birth and persisted for about a month and a half, following which it disappeared. The gain in weight was extremely slow even after the cessation of vomiting. There was no evidence of acute or chronic infectious processes. The Wassermann and tuberculin tests were negative. When transferred to the metabolism ward for study on Feb. 7, 1927, she weighed 6 pounds (2,727.5 Gm.). Her weight during the period of study is recorded in table 3, column 1. Although apparently in good condition and free from infection when she left the hospital on June 3, 1927, she was still very small, weighing only 9 pounds 5 ounces (4,224 Gm.). Subsequently she gained slowly. She finally developed pneumonia from which she died on Sept. 9, 1927. The diagnosis was confirmed at autopsy. The postmortem examination, however, did not reveal changes that might be considered to play a rôle in producing or maintaining marasmus.

Histories of the remaining patients were recorded in previous communications.[2]

EXPERIMENTAL DATA

The calorimeter data appear in table 1 and are arranged with the clinically normal infants at the top.

The amount of sugar excreted in the urine following the ingestion of dextrose was measured and recorded in table 1. In only a few instances was sugar found in the urine, and in these instances it was present in trivial amounts. None of the infants showed sugar in the urine during the intervals between studies.

Samples of blood were taken before and after the ingestion of food. The data appear in table 2.

How completely was the ingested dextrose absorbed by our patients? This question is asked by all workers who study the effect of the ingestion of measured amounts of dextrose. This question cannot, at present, be positively answered because part of the carbohydrate may undergo fermentation in the gastro-intestinal tract and thus be lost. Talbot and Hill,[9] Utheim,[10] Parsons [11] and Courtney [12] have found, however, that

9. Talbot, F. B., and Hill, L. W.: The Influence of Lactose on the Metabolism of an Infant, with Special Reference to Fat, Nitrogen and Ash, Am. J. Dis. Child. **8**:218 (Sept.) 1914.

10. Utheim, K.: Advanced Chronic Nutritional Disturbances in Infancy, J. Metab. Research **1**:803 (June) 1922.

11. Parsons, L. G.: Wasting Disorders of Early Infancy, Lancet **1**:687 (April 5) 1924; **1**:793 (April 19) 1924.

12. Courtney, A. M., quoted by Tisdall et al: Am. J. Dis. Child. **30**:829 (Dec.) 1925.

large amounts of carbohydrate may be fed to marasmic infants without an appreciable amount making its appearance in the stools. Tisdall [1] concluded that "there is no evidence from the examination of stools of marantic infants without diarrhea, that there is any excessive fermentation of carbohydrate and resultant production of organic acids." The work of Cori [13] with rats suggests that insulin does not affect the amount of dextrose absorbed.

In the absence of diarrhea and in the absence of significant quantities of sugar in the urine and in view of the work just cited, we have assumed that the ingested sugar was as completely absorbed in the marasmic as in the normal infant.

TABLE 2.—*Blood Analyses*

Case	Name	Experiment No.	Date	Blood: Sugar, Mg. per 100 Cc. Before* (1)	Blood: Sugar, Mg. per 100 Cc. After (2)	Blood: Carbon Dioxide, per Cent by Volume† Before* (3)	Blood: Carbon Dioxide, per Cent by Volume† After (4)	Time‡ Minutes (5)
				Control Infants				
2	C. H.	17	4/16/26	92.4	87.2	37.7	36.7	191
		18	4/19/26	123.7	....	31.4		
		24§	5/ 3/26	123.7	29.7¶	30.4	34.2	232
		25§	5/14/26	74.7	60.5	32.0	34.9	228
5	A. S.	54	1/19/27	73.4	110.1	30.0	27.9	216
		55§	1/21/27	77.6	116.9	24.5	27.6	159
				Marasmic Infants				
5	A. S.	28	10/22/26	....	179.7	....	32.4	196
		29§	10/25/26	34.5	50.1	28.3	33.5	162
		39	11/19/26	59.7	84.0	40.3	39.9	195
8	C. F.	48	12/29/26	52.2	177.8	27.3	37.7	202
		50	1/ 3/27	#	#			
		49§	12/31/26	53.7	82.1	23.9	25.1	215
10	V. O'B.	63	2/21/27	66.4	145.5	36.3	39.3	200
		65§	2/23/27	59.8	98.0	33.6	29.7	217

* Blood taken about four hours after a small meal.
† These determinations are volumes per cent content in whole blood.
‡ These figures represent the time interval between the ingestion of food and the withdrawal of the second sample of blood.
§ Experiments in which insulin was administered.
# Determination of blood sugar not done. Experiment 50 is a duplicate of experiment 48.
¶ This patient did not show twitchings or convulsive movements at any time during or after the observation period.

RESULTS

It would seem most logical first to consider the respiratory quotients, as further calculations are based on these figures.

The reliability of quotients was controlled in part by alcohol check experiments described earlier in this paper. They were further checked by determinations of carbon dioxide content made on blood samples taken at the beginning and at the end of experiments. We believe that the changes, as recorded in table 2, were probably unimportant and that

13. Cori, C. F., and Cori, G. T.: The Fate of Sugar in the Animal Body: II. J. Biol. Chem. **70**:557 (Oct.) 1926.

the quotients were not significantly affected by the blowing off or accumulation of carbon dioxide in the body during experiments.

Respiratory Quotients.—Following the ingestion of dextrose, there was invariably a marked elevation of the respiratory quotient in both normal and marasmic infants. The subcutaneous administration of insulin, prior to the ingestion of dextrose, did not produce consistent variations in the height to which the quotient was elevated. The elevation of the respiratory quotient following the ingestion of dextrose is entirely consistent with long accepted observations.

The respiratory quotient obtained in infants following the ingestion of small meals presumably approximates the basal quotient—it being impossible to secure true basal values because infants will not remain quiet for long periods without food. Such quotients are recorded in table 2 of paper VIII.[2] Consistent differences were not observed in the normal and the marasmic infants. This is corroborative of the work of Fleming and Hutchison.[14]

Actual Amount of Carbohydrate Burned.—The total carbohydrate oxidized by infants during observations show wide variations (table 3, column 4). These are largely due to differences in the duration of observations. For purposes of comparison, the average number of grams burned per hour was computed and recorded (table 3, column 5). With the elimination of the factor of time, variations in these figures were less marked. There is still, however, considerable variation in the different patients. This is apparently due to other factors which will be considered later in this paper.

On the basis of work done with rats, Cori [13] recently suggested that there is a maximum rate at which carbohydrate can be burned during rest following the ingestion of dextrose. Our data would likewise suggest this. Infant C. H., for example, in experiment 17, burned 2.9 Gm. of carbohydrate per hour after the ingestion of 22 Gm. of dextrose and in experiment 18, he burned 3.0 Gm. of carbohydrate per hour after the ingestion of 35 Gm. of dextrose. When somewhat older and heavier the same infant again burned in experiment 24, 3.2 Gm. of carbohydrate per hour after the ingestion of 27 Gm. of carbohydrate, and in experiment 25 he burned 3.3 Gm. of carbohydrate per hour after the ingestion of 35 Gm. of dextrose. The similarity of these figures would suggest that there is a maximum rate at which an infant can burn carbohydrate while at rest beyond which further additions to the amount ingested does not appreciably influence the rate of oxidation. Cori [13] concluded from observations on rats that there is a certain definite maximum rate of absorption of carbohydrate from the gastro-intestinal tract. If

14. Fleming, G. B., and Hutchison, H. S.: A Study of the Metabolism in the Undernourished Infant, Quart. J. Med. **17**:339 (July) 1924.

this holds true for infants, it may be that the rate of absorption plays a part in determining the maximum rate at which carbohydrate can be burned, but it is probable that other factors are also involved.

It is also of interest to compare the ability of our infants to burn carbohydrate with that of adults as reported by Sanger and Hun.[15] These workers found that ten normal adults burned an amount of carbohydrate equivalent to an average of 18.1 per cent of that ingested during a period of two and one-half hours after the ingestion of 1.75 Gm. of dextrose per kilogram of body weight. All of our infants ingested relatively larger amounts of dextrose per unit of body weight than did the adults of Sanger and Hun. The amount ingested ranged between 3 and 10 Gm. per kilogram of body weight. The proportion of ingested carbohydrate burned in a two and one-half hour period as computed from our data exceeded in every instance the maximum figure given by Sanger and Hun. The case of C. H. illustrates the point. Following the ingestion of 6.0 Gm. per kilogram of body weight, he burned 21.5 per cent of ingested carbohydrate, and with the ingestion of 4 Gm. per kilogram he burned 33 per cent of ingested dextrose. If amounts as low as 1.75 Gm. per kilogram had been given, the proportion burned would undoubtedly have been much higher. Calculated on the basis of surface area, differences between the amounts given to Sanger and Hun's adults and to our infants remain, but they are not as striking as when calculated on the basis of body weight.

The data of Sanger and Hun and our own data are not strictly comparable because of differences in the experimental procedure, but they at least suggest that infants burn carbohydrate at a faster rate than adults.

Several standards were used to compare the ability of normal and marasmic infants to burn carbohydrate, and with this in view we have recalculated the data in several ways, each of which is discussed under appropriate headings.

The Relation of Actual Body Weight to the Amount of Carbohydrate Burned.—The weight of the patient, the expected weight calculated on the basis of age and the percentage of deviation of the actual from the expected weight are recorded in table 3, columns 1, 2 and 3. The grams of carbohydrate burned per kilogram of actual body weight per hour are found in table 3, column 6.

The condition of the subjects varied from a normal state to extreme emaciation. In figure 1, the grams of carbohydrate burned per hour are plotted against the degree of undernutrition expressed in percentage. Although too few determinations are available for a curve to be plotted

15. Sanger, B. J., and Hun, E. G.: The Glucose Mobilization Rate in Hyperthyroidism, Arch. Int. Med. **30**:397 (Sept.) 1922.

accurately, the figure nevertheless exhibits a definite tendency; namely, that the amount of carbohydrate burned per unit of actual body weight per hour is increased with undernutrition.

It is estimated from this figure that normal infants may burn, after the ingestion of dextrose, about 0.5 Gm. of carbohydrate per kilogram per hour and that infants who are 50 per cent underweight burn in the neighborhood of 0.7 Gm. of carbohydrate per kilogram per hour. Additional determinations would permit the plotting of a smoothed curve

TABLE 3.—*Relation of Body Weight to Amount of Carbohydrate Burned*

						Carbohydrate, Grams					
								Per Kg. per Hour of			
Case	Name	Experiment No.	Weight, Kg. (1)	Expected Weight for Age, Kg.* (2)	Deviation, per Cent (3)	Total (4)	Per Hour (5)	Actual Body Weight (6)	Expected Weight for Age (7)	Computed Weight (100/70 × Weight) (8)	Surface Area per Sq. Meter per 24 Hours (9)
					Control Infants						
1	J. B.	3	6.11	5.53	+10	4.6	3.0	0.49	0.54	....	8.8
		7	6.22	5.71	+ 9	5.9	3.0	0.48	0.53	....	8.6
2	C. H.	17	5.67	6.53	—13	5.8	2.9	0.51	0.45	....	9.2
		18	5.68	6.53	—13	6.2	3.0	0.53	0.46	....	9.5
		24†	5.78	6.83	—15	6.4	3.2	0.56	0.47	....	9.9
		25†	6.01	6.97	—14	6.5	3.3	0.54	0.47	....	9.9
5	A. S.	54	6.24	8.21	—24	8.4	3.7	0.60	0.45	....	10.9
		55†	6.28	8.21	—24	4.9	3.9	0.63	0.48	....	11.6
					Marasmic Infants						
5	A. S.	28	3.47	6.83	—49	6.3	2.8	0.80	0.41	0.56	12.2
		29†	3.64	6.83	—48	4.1	2.7	0.75	0.39	0.52	11.5
		39	4.23	7.36	—43	7.4	2.9	0.70	0.40	0.49	11.3
8	C. F.	48	4.76	9.00	—47	3.8	3.0	0.64	0.34	0.45	10.8
		50	4.76	9.06	—47	7.0	3.5	0.74	0.38	0.52	12.4
		49†	4.76	9.00	—47	6.6	3.3	0.69	0.37	0.48	11.7
10	V. O'B.	63	2.75	5.89	—53	4.5	1.8	0.66	0.31	0.46	9.2
		65†	2.78	5.89	—53	5.3	2.0	0.71	0.34	0.50	10.2

* Woodbury, R. M.: Statures and Weights of Children under Six Years of Age, U. S. Department of Labor, Children's Bureau, publication 87, 1921.
† Experiments in which insulin was used.

from which the expected consumption of carbohydrate after large feedings of carbohydrate could be calculated from the patients' weight and age.

The amounts of carbohydrate burned after the subcutaneous administration of insulin are included in figure 1. Perusal of this figure reveals the fact that the amount of carbohydrate burned after the use of insulin approximates that burned when insulin was not administered. Demonstrable consistent difference is not apparent. The results of experiments with insulin seem to indicate that the carbohydrate metabolism of the marasmic infant is not impaired.

Woodyatt, Sansum and Wilder [16] and Mattill, Mayer and Sauer [17] and others have estimated the amount of dextrose that can be tolerated by adults and by normal and marasmic infants when injected intravenously. These values represent the amount of dextrose that can be burned and stored. Our determinations, in a measure, supplement these calculations. An examination of figure 1 indicates that carbohydrate

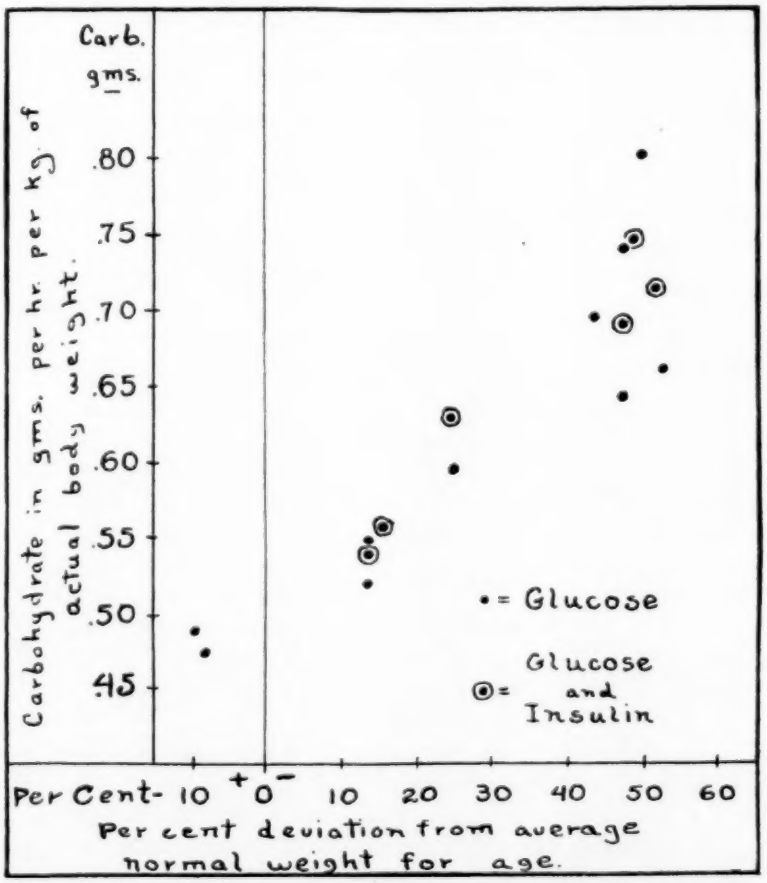

Fig. 1.—The relation of grams of carboyhydrate oxidized per hour and per kilogram of actual body weight, to the degree of nutrition expressed as percentage deviation from the average normal weight for age.

16. Woodyatt, R. T.; Sansum, W. D., and Wilder, R. M.: Prolonged and Accurately Timed Intravenous Injection of Sugar; A Preliminary Report, J. A. M. A. **65**:2067 (Dec. 11) 1915.

17. Mattill, P. M.; Mayer, K. M., and Sauer, L. W.: Dextrose Tolerance in Atrophic Infants, Am. J. Dis. Child. **19**:42 (Jan.) 1920.

can be burned by the normal infant to the extent of about 0.5 Gm. per kilogram of body weight per hour after the administration of dextrose by mouth.

The Relation of Expected Weight for Age to the Amount of Carbohydrate Burned.—The amount of carbohydrate burned per unit of expected weight for age is recorded in table 3, column 8. Figure 2 is a graphic representation in which these figures are plotted against the degree of undernutrition expressed in percentage.

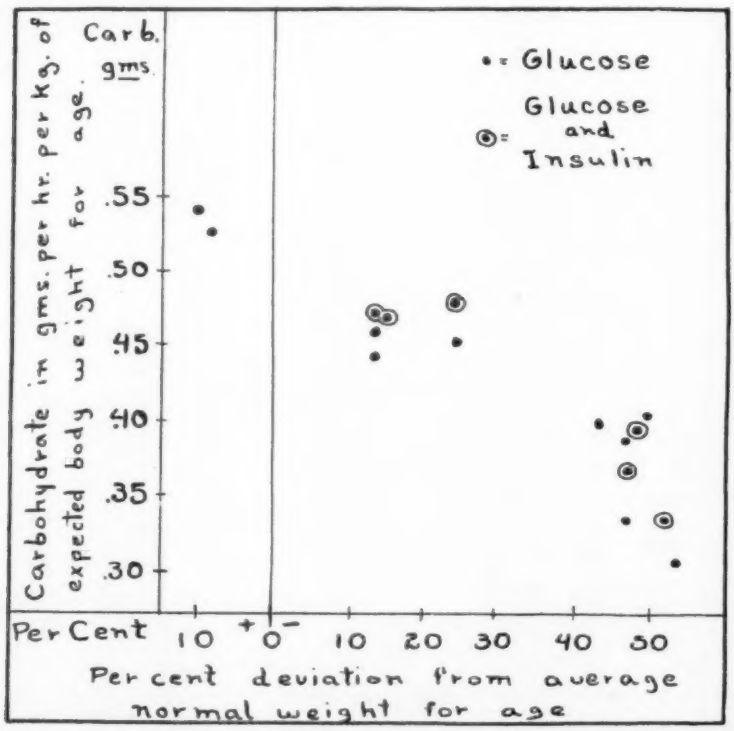

Fig. 2.—The relation of grams of carbohydrate oxidized per hour and per kilogram of expected body weight for age, to the degree of nutrition expressed in percentage deviation from normal weight for age.

The control infants in whom the actual and the expected weight approximated each other or, in other words, when the actual weight was approximately normal for age, the patient burned nearly 0.5 Gm. of carbohydrate per kilogram per hour. In patients whose weight varied from + 10 per cent to — 24 per cent of the normal for their age, the carbohydrate metabolized varied between 0.45 and 0.54. Marked undernutrition was associated with a considerable decrease in the quantity of carbohydrate metabolized per unit of expected weight.

The fact that the marasmic infants burned less carbohydrate per unit of expected weight than normal infants might lead one, on first thought, to suspect the possibility of a diminished ability to oxidize carbohydrate. However, the relative value of calculations based on the expected weight for age must be considered. In the case of marked undernutrition of long duration, there is usually a recognizable slowing of growth as indicated by body height. Not only is the skeleton smaller and the fat depots depleted, but the metabolically active musculature is probably also diminished as compared with that of the normal infant.[18] For this reason it would obviously be unfair to compare the relative efficiency of carbohydrate utilization in normal and marasmic infants on the basis of the amount burned per unit of expected weight for age.

The subcutaneous administration of insulin did not produce any consistent effect on the oxidation of carbohydrate as recalculated on the basis of expected weight for age. Figure 2 shows the similarity of results between the experiments with insulin and the corresponding ones without insulin.

Relation of the Computed Weight (100/70 × Body Weight) to the Amount of Carbohydrate Burned.—In a preceding paper,[2] it was assumed that 30 per cent of the total body weight of the normal infant is composed of metabolically inert fat tissue. It was further assumed that 100/70 of the body weight of a marasmic infant gives a figure that is equivalent to the weight of the patient if a normal amount of inactively metabolic fat tissue were present. The evidence on which these assumptions rest were presented in paper VIII.

If these assumptions are accepted and the amount of carbohydrate burned per kilogram per hour by the marasmic infants is recalculated on this basis, it is found that the amount of carbohydrate burned per unit of computed weight falls within the limits of that calculated for normal infants. This fact is graphically illustrated in figure 3.

These observations suggest, first, that the carbohydrate burned by infants is dependent on their actively metabolic tissue, and, second, granting the validity of our assumption, that the carbohydrate is burned equally well in normal marasmic infants. Apparent differences are eradicated when calculations are made on the basis of computed weight (100/70 actual weight).

Furthermore, it was found that the amount of carbohydrate oxidized after the subcutaneous administration of insulin fell close to the amount burned when insulin was not given. This suggests again that insulin is neither required nor indicated in the treatment of marasmic infants.

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18. This statement probably holds for infants more than 30 per cent under the average normal weight for age. When the undernutrition is less than this, the diminution in weight is in all probability chiefly at the expense of metabolically inert fat tissue.

The maximum rate of carbohydrate combustion by marasmic infants may be roughly estimated in grams of carbohydrate per kilogram per hour by multiplying 100/70 of the actual weight by 0.5 Gm., which represents the amount burned by normal infants per kilogram per hour.

The Relation of Surface Area to the Amount of Carbohydrate Burned.—The carbohydrate metabolized by normal and marasmic infants per square meter of body surface showed wide variations (table 3, column 8). These discrepancies may be explained in part by the possible errors in the present method of estimating surface area, especially in

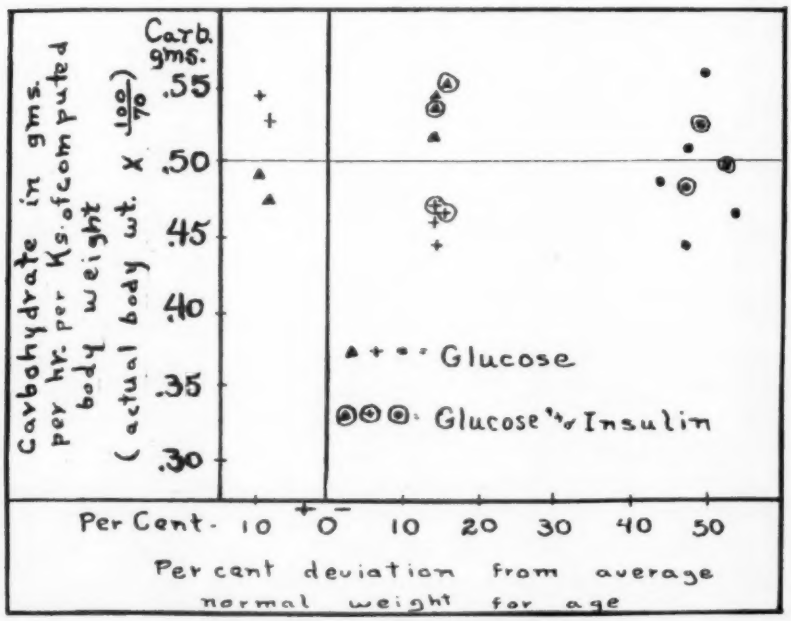

Fig. 3.—The relation of grams of carbohydrate oxidized by marasmic infants 30 per cent or more underweight, per hour per kilogram of computed weight (100/70 times the body weight), to the degree of undernutrition expressed in percentage deviation from the normal weight for age. The determinations indicated by the black triangles and + were not calculated in the foregoing manner, for these subjects were clinically normal and were within ± 15 per cent of normal weight for age. The black triangles indicate controls calculated on the basis of actual weight; +, controls calculated on basis of expected weight for age and the black dots, marasmic infants calculated on basis of computed weight.

marasmic infants. The amount of carbohydrate oxidized by each infant following the administration of insulin does not appreciably differ from that oxidized without insulin. These results do not afford any evidence for the efficacy of insulin as a therapeutic agent in marasmus.

Effect of Insulin.—It is apparent from studies on animals which have been recently reviewed by Chaikoff and Macleod,[19] that many factors influence the metabolism of carbohydrate and that the results vary when different species of animals are used. For example, Cori [13] found that combustion of dextrose was increased in rats by the administration of insulin. Chaikoff and Macleod,[19] on the other hand, found that when insulin was given to rabbits which had received continued feedings of carbohydrate, it did not cause significant increase in the amount of carbohydrate burned as reflected by the oxygen consumption and the respiratory quotient.

In the case of infants we can merely restate the results of our determinations, for too many factors are involved to warrant definite conclusions. We did not find a consistent change in the carbohydrate metabolized by normal and marasmic infants following a large dextrose meal when preceded by a subcutaneous injection of insulin.

Determinations of blood sugar are recorded in table 2. They are too few to permit of conclusions and were not intended to be more than accessories to our main experimental procedures with the respiration calorimeter. They are, however, consistent with the observations of other workers.

The blood sugar of the marasmic infants was lower than that of normal controls in all but one instance. This fact was previously shown by Cobliner [20] in 1911, and by other workers more recently. The ingestion of dextrose caused an elevation of blood sugar in both normal and marasmic infants. The administration of insulin lowered the blood sugar after the ingestion of dextrose in both marasmic infants and normal controls. Individual variations in these experiments were marked and depended on several factors, i.e., time interval, ingested dextrose, amount of insulin administered and perhaps other factors. The determinations of blood sugar at the close of the experiment are therefore only partially comparable. Available data, however, do not suggest any new fundamental differences between the marasmic and normal infants following the ingestion of dextrose.

COMMENT

We believe that the data presented in this paper add a few new facts to the sum total of those known about carbohydrate metabolism in infants. As stated in the first part of this paper, Tisdall, Drake and Brown [1] have recently reviewed the subject of carbohydrate metabolism

19. Chaikoff, I. L., and Macleod, J. J. R.: The Effect of Insulin on the Respiratory Exchange of Fed and Fasting Rabbits, J. Biol. Chem. **73**:725 (June) 1927.

20. Cobliner, S.: Blutzuckeruntersuchungen bei Säuglingen, Ztschr. f. Kinderh. **1**:207, 1911.

in normal and marasmic infants. For this reason, it is unnecessary to go into a detailed discussion.

It has been shown that marasmic infants have a lower fasting blood sugar than normal infants.[20] The work of Tisdall and others [1] suggests that dextrose is removed from the blood stream of marasmic infants more rapidly than from that of normal infants. On the assumption that there might be a defect in the carbohydrate metabolism of marasmic infants, insulin was proposed and used as a therapeutic agent. It was first suggested for this purpose by Pitfield.[21] Later, Marriott [22] concluded that intravenous injections of insulin and dextrose might improve the nutrition of marasmic infants. Since then, a large number of other observers have published the results of their work. The evidence brought forward by the various workers is conflicting.

The previously accumulated data which fail to support the view that there is a disturbance of carbohydrate metabolism in marasmus were also reviewed by Tisdall.[1]

The results of our investigations as recorded in this paper are based on studies of the intermediary metabolism following the ingestion of dextrose. The amount of carbohydrate burned by normal and marasmic infants was compared in several ways, in none of which could any evidence be found suggesting that there was a defect in the ability of the marasmic infant to burn carbohydrate. Further evidence was found in the fact that appreciable differences could not be observed between the amounts burned by the infants when they received insulin and when they did not.

SUMMARY

1. The carbohydrate metabolism as reflected by consumption of oxygen and the respiratory quotient was studied in normal and marasmic infants following the ingestion of a large dextrose meal—both with and without the previous subcutaneous administration of insulin.

2. A study of the relation of actual body weight to the amount of carbohydrate oxidized indicates that normal infants may burn about 0.5 Gm. of carbohydrate per kilogram per hour after the ingestion of a large dextrose meal.

3. Marasmic infants burn, on the basis of actual weight, more carbohydrate than normal infants; in other words, they burn more than 0.5 Gm. per kilogram per hour.

4. Marasmic infants burn, on the basis of expected weight for age, less carbohydrate than normal infants; in other words, they burn less than 0.5 Gm. per kilogram per hour.

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21. Pitfield, R. L.: On the Use of Insulin in Infantile Inanition, New York M. J. **118**:217 (Aug.) 1923.

22. Marriott, McKim. W.: The Food Requirements of Malnourished Infants with a Note on the Use of Insulin, J. A. M. A. **83**:600 (Aug. 23) 1924.

5. When the carbohydrate metabolized by marasmic infants was calculated on the basis of computed weight (100/70 of actual weight), it was found that the marasmic infants oxidized nearly 0.5 Gm. of carbohydrate per kilogram per hour. This suggests that carbohydrate combustion in an infant at rest following the ingestion of a large dextrose meal is dependent on the amount of actually metabolic protoplasmic tissue contained in that infant.

6. A striking uniformity of results was not observed when the amount of carbohydrate metabolized was compared in different persons on the basis of surface area.

7. The amount of carbohydrate burned by normal and marasmic infants was essentially the same whether insulin was or was not previously administered.

8. The evidence suggests that there is a certain constant maximum rate at which carbohydrate can be burned during rest following the ingestion of large dextrose meals.

9. The rate of oxidation of carbohydrate in infants is apparently faster than in adults under essentially similar conditions.

CONCLUSIONS

1. The evidence obtained from this study suggests that there is not a fundamental difference in carbohydrate metabolism between normal and marasmic infants.

2. The absence of any demonstrable defect of carbohydrate metabolism in marasmic infants suggests that the use of insulin as a therapeutic agent in marasmus is not indicated.

161 West Sixty-First Street.

THE RÔLE OF HEMOLYSIS IN JAUNDICE OF THE NEW-BORN INFANT*

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In 1882, Hofmeier [1] first suggested a hematogenous origin for jaundice of the new-born infant. For years this theory received little attention, but evidence gradually accumulated which led writers on the subject to grant it a rôle of minor importance, then to assign it a parity with hepatogenous factors, and finally to advance it as the sole cause of this condition.

In 1912, Hess [2] dismissed blood destruction as being a primary cause of jaundice, on the following grounds: First, when the liver is extirpated, jaundice cannot be induced; second, the finding of bile acids in the pericardial fluid of jaundiced babies proves the participation of the liver; third, free hemoglobin cannot be found in the blood of the new-born infant; fourth, jaundice cannot be produced by the injection of hemoglobin, and fifth, jaundice does not follow transfusion. Today each of these objections can be met. Whipple and Hooper [3] proved that the failure of Minkowski and Naunyn [4] to produce jaundice in geese in which they had removed the liver did not hold for mammals; then Mann [5] proved conclusively that jaundice could be produced in the absence of not only the liver but all the abdominal viscera. Whipple and Hooper have also shown that bile pigment and bile acid excretion are separate and independent functions of the liver which do not parallel each other. In 84 of 118 cases of jaundice, Haselhorst and Papendieck [6] found hematin (an isomer of hemoglobin) in the serum of new-born

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1. Hofmeier: Ztschr. f. Geburtsh. u. Gynäk. **8**:278, 1882.

2. Hess, A. F.: A Study of Icterus Neonatorum by Means of the Duodenal Catheter, Am. J. Dis. Child. **3**:304 (May) 1912.

3. Whipple, G. H., and Hooper, C. W.: Icterus—A Rapid Change of Hemoglobin to Bile Pigment in the Circulation Outside the Liver, J. Exper. Med. **17**: 593, 1913.

4. Minkowski, O., and Naunyn, B.: Arch. f. exper. Path. u. Pharmakol. **21**: 1, 1886.

5. Mann, F. C.; Bollman, J. L., and Magath, T. B.: The Formation of Bile Pigment After Total Removal of the Liver, Am. J. Physiol. **69**:393, 1924; **76**:306, 1926.

6. Haselhorst, G., and Papendieck, A.: Hämatin als physiologischer Bestandteil des Blutes in der Fötalperiode und bei Neugeborenen, Klin. Wchnschr. **3**: 979, 1924.

infants. This hematinemia was nearly always present during the first days of life and gradually disappeared during the second week. Mann has shown that the intravenous injection of laked blood will cause an acceleration of jaundice in dogs with extirpated livers. It is a matter of common knowledge that jaundice may follow the transfusion of blood from an incompatible donor.

Following the introduction of the van den Bergh test [7] and its general acceptance as a means of differentiating obstructive and nonobstructive jaundice, it was thought that its application to icteric new-born infants would finally settle the hematogenous or hepatogenous origin of this form of jaundice. Some writers (Rolleston,[8] Kramer,[9] Klemperer,[10] Lepehne,[11] Williamson [12] and others) have accepted the results obtained by this method as conclusive proof of a hematogenous origin. A few recent investigators have cast doubt on the validity of this mode of differentiation, but many more have confirmed it.

By the use of cord blood, Knöpfelmacher and Kohn [13] in fifty cases, Cserna and Liebmann [14] (thirty-four cases), Zamorani [15] (four cases) and Kramer [9] (100 cases) found bilirubin increased by the indirect van den Bergh reaction in all cases and the direct reaction not positive in a single case. By the use of the blood taken from the new-born infant, Knöpfelmacher and Kohn (five cases) and I (forty-three cases reported in this article) found a positive indirect and a negative direct reaction in all cases. Schiff and Färber [16] found the indirect reaction positive in twenty-six of twenty-seven cases and both direct and indirect in one; they had diagnosed this case as familial icterus gravis. Knöpfelmacher found a positive direct reaction from bile taken from the gallbladder in three stillborn infants in whom the blood gave only an

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7. Hymans, van den Bergh, A. A.: Der Gallenfarbstoff im Blute, Leiden.

8. Rolleston, H.: Jaundice in the New Born, Practitioner **109**:1, 1922.

9. Kramer, P. H.: Jaundice in New-Born, Nederl. Tijdschr. v. Gennesk. **1**: 249, 1926; abstr., J. A. M. A. **86**:991 (March 27) 1926.

10. Klemperer, P.: Icterus Gravis of the New Born, Am. J. Dis. Child. **28**: 212 (Aug.) 1924.

11. Lepehne, G.: Pathologie des Ikterus, Ergebn. d. ges. inn. Med. u. Kinderh. **20**:221, 1921. Zur Kenntniss des Icterus neonatorum, Monatschr. f. Geburtsh. u. Gynäk. **60**:277, 1922.

12. Williamson, A. C.: Placental Iron and Its Relationship to Icterus Neonatorum, Surg. Gynec. Obst. **37**:57, 1923.

13. Knöpfelmacher, W., and Kohn, C.: Untersuchungen über den Gallenfarbstoff beim Icterus neonatorum, Monatschr. f. Kinderh. **22**:1, 1921.

14. Cserna, S., and Liebmann, S.: Beitrage zur Lehre des Icterus neonatorum, Klin Wchnschr. **2**:2122, 1923.

15. Zamorani: Le piu recenti vedute sulla bilirubinogenesi in rapporto coll' ittero dei neonati. Riv. di clin. pediat. **21**:385, 1923.

16. Schiff, E., and Färber, E.: Beitrage zur Lehre des Icterus neonatorum, Jahrb. f. Kinderh. **97**:245, 1922.

indirect reaction. Hoffman reported one case of proved obstructive jaundice in a new-born infant which gave a direct reaction. Grulee [17] disagrees with these observations in that two cases of catarrhal jaundice gave only an indirect reaction and one of obstructive jaundice gave irregular results.

The work of Hirsch,[18] Yllpö,[19] and Schiff and Färber [16] on the bilirubin content of the blood of new-born babies threw much new light on the subject. The results of their investigations showed: 1. The amount of bilirubin is higher in cord serum than in the adult or in the infant after jaundice has subsided. 2. The amount of bilirubin increases after birth, reaches a maximum between the first and seventh day and then subsides. 3. The degree of jaundice and the amount of bilirubin are parallel. 4. Bilirubin in cord blood is the same for premature and full term babies.

The source of the bilirubin has proved the point of contention. That it does not pass the placenta and so have origin in the mother seems proved. Turolt and Teyner [20] showed normal amounts of bilirubin in the blood of mothers when there was an increase in that of their babies at birth. They likewise observed one jaundiced mother whose blood contained a much higher amount of bilirubin than did that of her baby.

Yllpö placed the origin of the bilirubin in liver insufficiency, arguing largely from the greater incidence and intensity of jaundice in premature infants. Hallez [21] and Greil [22] attributed it to an exaggerated hemolysis of the blood cells, coupled with a temporary overburdening of a normal liver. Schick [23] advanced as its source blood pigment furnished by the mother from blood of the intervillous spaces or from extravasations in the placenta, thus localizing the origin in the latter organ. Schwartz,[24] Kramer,[9] and Cserna [14] all placed its origin in blood destruction, and the last named added the placenta as the organ of its excretion. Several investigators attempted to settle the question of whether bilirubin has its

17. Grulee, C. G., and Mebane, A.: The van den Bergh Test for Icterus in the Blood of Infants, Am. J. Dis. Child. **30**:219 (Aug.) 1925.

18. Hirsch, Asa: Die physiologische Ikterusbereitschaft des Neugeborenen, Ztschr. f. Kinderh. **9**:196, 1913.

19. Yllpö, Arvo: Icterus neonatorum und Gallenfarbstoffsekretion beim Foetus und Neugeborenen, Ztschr. f. Kinderh. **9**:208, 1913; Icterus neanatorum, Ergebn. d. ges. Med. 1924, vol. 5.

20. Turolt, M. A., and Teyner, O.: Beitrage zur Genese des Icterus neonatorum, Zentralbl. f. Gynäk. **47**:1618, 1923.

21. Hallez, G. L.: Nouvelles recherches sur l'ictere simple du nouveau-ne, Nourrisson. **13**:297, 1925.

22. Greil, A.: Entstehung und Vermütung des Icterus neonatorum, Ztschr. f. Geburtsh. u. Gynäk. **88**:628, 1925.

23. Schick, B.: Der Icterus neonatorum als Folge des Abhanes mütterlichen Blutes, Ztschr. f. Kinderh. **27**:231, 1921.

24. Schwartz, P.: Zur Frage des Icterus Neonatorum, Ztschr. f. klin. Med. **100**:117, 1924.

origin in the placenta or in the fetus by determinations on blood taken from the placental and fetal ends of the cord, respectively. By the use of the umbilical artery and vein, Turolt and Teyner [20] showed that first one, then the other, gave higher results, with a slight preponderance in blood coming from the placenta. They argued with force that both placenta and the fetus must be implicated.

Schwartz attacked the problem by a different method. With the acknowledged relationship of hemoglobin and iron as a starting point, he argued that if icterus neonatorum is due to blood destruction, there should be a concomitant change in iron deposits. As a result of his work with Baer and Weiser,[25] he showed that just as the bile pigments in the blood, so iron in the liver and spleen follows a typical curve which rises from the time of birth, reaches a maximum and then slowly falls reaching the original level by the fifth or sixth month.

His figures held for both premature and full term infants. Kruger [26] found, however, that the iron content of the fetal liver reached a maximum from three to four weeks before full term and from then on to delivery fell rapidly. The placenta, then, as the first site of the transformation of maternal blood, should be particularly rich in iron in the premature child. This Wagner [27] found to be true. Extending this work, Williamson [12] found that not only did all placentas contain iron, but the amount was proportionate to the degree of jaundice developing later.

If blood destruction is to be held accountable for the production of jaundice, whether directly or through intervention of the liver; and if this destruction occurs after birth, as seems indubitable from the fact that jaundice develops and bilirubin and iron both show great increase in that period, then the effects should be reflected in the blood count of the new-born infant. Hofmeier [1] maintained that such was the fact. His assertion was supported by the observations of Schiff,[28] Fehrsen,[29] Heimann,[30] Takasu [31] and Williamson,[32] using as an index hemoglobin

25. Schwartz, P.; Baer, R., and Weiser, J.: Histologische Untersuchungen über den Eiweiszstoffwechsel im frühen Säuglingsalter, Ztschr. f. Kinderh. **37:** 167, 1924.

26. Kruger, quoted by Wagner (footnote 27).

27. Wagner, R.: Icterus neonatorum und Eisengebalt der Placenta, Ztschr. f. Kinderh. **27:**251, 1920.

28. Schiff, E.: Neure Beitrage zur Haemotologie der Neugeborenen mit besonderer Rüchsicht auf die Abnabelungzeit, Jahrb. f. Kinderh. **34:**159, 1892.

29. Fehrsen, A. O.: The Hemoglobin and Corpuscular Content of the Blood of the Newborn, J. Physiol. **30:**322, 1903.

30. Heimann, F.: Zur Lehre des Ikterus neonatorum, Ztschr. f. Geburtsh. u. Gynäk. **69:**165, 1911.

31. Takasu, K.: Blutuntersuchungen bei den Japanischen Kindern, Arch. f. Kinderh. **39:**436, 1904.

32. Williamson, C. S.: Influence of Age and Sex on Hemoglobin, Arch. Int. Med. **18:**505 (Oct.) 1916.

determination. They all showed consistently high readings at birth, which rapidly fell to below the adult normal. Aitkin,[33] Perlin,[34] Williamson,[12] Ziegelroth[35] and Greil[22] made similar observations concerning the red blood count, but Lucas,[36] although he found a slight drop in both the hemoglobin and red blood count during the first few days of life, was unable to find any difference in infants with or without jaundice. Lippmann,[37] who made an exhaustive study, found that there was a rapid rise in the red blood count in the first six hours of life, followed by a fall to approximately birth level, which persisted to forty-eight hours. He did not find any relation between the blood count and the loss of weight in the first two days. In five cases of jaundice there was no change from the general observations, but his studies went only as far as the first forty-eight hours of life. That there is excessive function and production of the hematopoietic system of the new-born infant, however, was shown by Lippmann on the basis of cell morphology, and Greil[22] has added that in the icteric young, immature, nucleated red cells number from 12,000 to 16,000 per million instead of from 100 to 1,200 per million as in normal persons; the leukocyte count is also high. A quantitative relationship between blood destruction and jaundice has not been demonstrated, but Rosenthal and Meier[38] were able to produce icterus by the injection of hemolyzing dyes, and McMaster[39] found that any condition leading to blood destruction gave rise to increased excretion of bile pigment from the liver.

In familial hemolytic jaundice resistance of the red blood cells to hypotonic salt solution is diminished, whereas in obstructive jaundice the resistance is increased. Hornung[40] found an increased osmotic resistance of the red blood cells in new-born infants, which was especially pronounced in the icteric. He believed that this testified against a hemolytic origin of icterus neonatorum. In thirty-one new-born infants,

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33. Aitkin, J.: Blood Counts in the New Born, J. Obst. and Gynec. Brit. Emp. **1**:414, 1902.

34. Perlin: Jahrb. f. Kinderh. **58**:549, 1903.

35. Ziegelroth, P.: Altitude Polycythemia and Jaundice of New Born, München med. Wchnschr. **73**:1440, 1926; abstr., J. A. M. A. **87**:1782 (Nov. 20) 1926.

36. Lucas, W. P.; Dearing, B. F.; Hoobler, H. R.; Cox, A.; Jones, M. R., and Smyth, F. S.: Blood Studies in the New Born, Am. J. Dis. Child. **22**:525 (Dec.) 1921.

37. Lippmann, H. S.: A Morphologic and Quantitative Study of the Blood Corpuscles in the New Born Period, Am. J. Dis. Child. **27**:473 (May) 1924.

38. Rosenthal and Meier: Arch. f. exper. Path. u. Pharmakol. **91**:246, 1921.

39. McMaster, P.; Broun, G., and Rous, P.: Studies on the Total Bile, J. Exper. Med. **37**:395, 1923.

40. Hornung: Erythrozytenresistenz und Cholesteringehalt des Neugeboren blutes, Klin. Wchnschr. **4**:475, 1925.

Hallez [21] found a decreased minimum resistance and an increased maximum resistance. The latter he felt was due to the increased number of young cells in the blood. Pollitzer [41] did not find a great difference in the resistance of nonicteric new-born infants and infants several months old. In icteric infants the resistance was found to be normal, decreased or increased. The last he also attributed to the presence of the young forms.

Pollitzer added to his investigation of fragility, that of hemolysis. He found that he was able to demonstrate isolysins in a few icteric new-born infants. These were lacking in those jaundiced, new-born babies with decreased resistance of the erythrocytes, in which cases he assumed them to be fixed to the red blood cells. The presence of autolysins was transitory.

In conjunction with Rapisardi,[42] Pollitzer tested the hemolyzing power of the serum in twenty-five mothers and their babies. In seven of the twenty-five cases, the mother's blood hemolyzed the blood of the baby. The serum of the infant did not hemolyze the cells of the mother. No reference was made to whether or not the subjects were icteric.

Dogliotti [43] also tested hemolysis between mother and child. The serum of new-born infants failed to hemolyze the red blood cells of any person. Of fifty cases examined, the mother's serum hemolyzed the red blood cells of her new-born infant in six cases in a dilution of 1 : 10 and in five cases in a dilution of 1 : 100. The titer was lower and the proportion of positive cases much less in older children. The father's serum hemolyzed in the same number, five cases, 1 : 10, and in four cases, 1 : 80. Persons outside the family hemolyzed fourteen of fifty cases. Hemolysis and agglutination ran parallel. No reference was made to the presence or absence of jaundice or the comparative blood groups.

Luska [44] reported in the blood serum of eleven icteric new-born infants a hemolytic agent closely resembling a staphylolysin. A rise of antistaphylotoxic titer was present in all cases. He concluded that jaundice of the new-born infant was due in these cases to a bacteriotoxic hemolysis caused by a hemolytic staphylococcus.

Schwartz,[24] Deluca [45] and others have felt that in blood extravasated at birth due to the trauma associated with delivery lay the origin of jaundice. As of major importance this statement is scarcely borne out

41. Pollitzer, R.: Contributo statistico ericerche sulla patogenesi dell'ittero dei neonati, Pediatria. **32**:69, 1924.

42. Rapisardi, S., and Pollitzer, R.: Pediatria **32**:916, 1924.

43. Dogliotti: Clin. chir. **29**:901, 1926.

44. Luska, F.: Pathogenesis of Icterus of New-Born, Čas. lék. česk. **61**:1, 1922; abstr., J. A. M. A. **78**:932 (March 25) 1922.

45. Deluca, F. A.: Rev. franc. de gynéc. et d'obstét. **16**:641, 1921.

by Hilgenberg,[46] who made a careful statistical study of 564 cases. In these there were forty-nine who showed marked evidences of birth traumas, 78 per cent of whom later developed jaundice, his entire series showing a jaundice incidence of 68 per cent.

TECHNIC

The main experiment was designed to show whether the mother's serum and that from the cord would hemolyze the red blood cells of the infant and if so whether there was any relation between such hemolysis and the presence of jaundice; Bourquin[47] and Kreidly and Mandl[48] have shown that hemolysins can pass the placenta.

Hemolysis tests were performed once a week. All procedures were carried out under sterile precautions up to the time of actual performance of the test. At birth, cord blood was collected and allowed to stand until the following morning, when the serum was pipetted off. This serum was then kept in the ice-box until the day of the next test.

Blood was collected by venipuncture from the mother, a dry syringe being used. It was allowed to stand for one hour, then the serum was removed and kept at room temperature until the following morning (averaging twenty hours). The cells of the babies were collected in 2 per cent sterile sodium citrate in sodium chloride solution by pricking the skin of the heel which previously had been cleaned thoroughly with alcohol and dried. The cells were immediately centrifugalized and washed three times in sodium chloride solution, and a 5 per cent suspension in sodium chloride solution was made. The tests were performed at once.

Serums were diluted with sodium chloride solution, and 5 per cent cell suspension was added in equal amount (0.5 cc.) in such a manner as to make the final serum dilutions 1:2, 1:4, 1:8, 1:16, 1:32, 1:64. These were shaken thoroughly, incubated for ninety minutes at 37 C. and read.[49] Controls of saline and cells and of saline and serum were used. Any serum which showed evidences of hemolysis prior to the introduction of cells was discarded.

Van den Bergh[50] tests were performed in fifty-eight cases; forty-three on infants' blood and fifteen on cord blood. Cord blood was obtained as described. Blood was collected from the babies by venipuncture, in a dry sterile syringe, and the serum was pipetted off either following immediate centrifugalization at slow speed or after standing at room temperature for one hour. Tests were per-

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46. Hilgenberg, F. C.: Statisticher Beitrag zur Frage des Icterus neonatorum simplex, Monatschr. f. Geburtsh. u. Gynäk. **68**:326, 1925.

47. Bourquin, H.: A Study of the Permeability of the Placenta: I. Permeability to Agglutinins, Hemolysins, Am. J. Physiol. **59**:122, 1922.

48. Kreidly and Mandl, quoted by Hofbrauer, J.: Ztschr. f. Geburtsh. u. Gynäk. **64**:668, 1909.

49. Readings were checked by Dr. Frank Lynch of the Pepper Laboratory. Check readings were allowed to stand since Dr. Lynch was not familiar with the cases clinically.

50. The van den Bergh tests were performed by Mr. J. P. Taylor of the Chemical Division, Pepper Laboratory.

formed on the same day the specimen was taken in most instances, always within twenty-four hours. The technic used was that described by Ravdin.[51]

A small series of fifteen fragility tests were made, nine in jaundiced and six in nonjaundiced cases. Blood was collected by venipuncture in a dry syringe on the same day that the hemolysis tests were made. One drop of whole blood was put immediately into chemically clean but not sterile test tubes containing 1 cc. each of salt solutions made up in the standard dilutions of 0.625, 0.600, 0.575, 0.550, 0.525, 0.500, 0.475, 0.450, 0.425, 0.400, 0.375, 0.350, 0.325, 0.300, 0.275 and 0.250. These were allowed to stand for sixty minutes at room temperature and then read.

The blood group of the mother was determined in every case in which an hemolysis test was performed. Both serum and cells were used in making this determination.

An attempt was made to determine the blood group of the infant in a total of 141 cases. For this purpose, cord blood was collected at the time of delivery. The following morning blood was obtained by pricking the skin of the toe of the infant and collected in 2 per cent sterile sodium citrate in sodium chloride solution. The group of the serum and the cells was then determined by the microscopic method, the procedure recommended by Jones[52] being employed with a few minor changes. Readings were made immediately and at the end of thirty minutes' incubation at 37 C. Stock serum of groups II, III and IV (Moss) were used. Cells from donors of known groups II and III were collected in citrate and used for several days.

Determination of the group of the infant's cells was attempted the morning following birth and at frequent intervals thereafter until discharge or definite establishment of the group. Serum readings were made at birth on the cord blood and from blood collected by venipuncture at weekly intervals thereafter until the infant was discharged from the hospital.

Most writers have agreed that jaundice is first observed about the nostrils and mouth and then on the back and that only in the more marked cases does it appear in the sclerae. In this series the sclerae were used as the final criterion, because it was found that in no case in which by virtue of the color of the skin it was felt undeniably justifiable to call the baby jaundiced was there not also discoloration of the sclerae, provided these were carefully examined in good light. Special care was taken on account of the hemolysis experiment not to include in the jaundiced group any case in which any one would question the presence of jaundice. This may have led to a slightly lowered incidence in the series. For purposes of classification, jaundice was recorded as + or ++, +++ and ++++, corresponding respectively to slight, moderate, and marked jaundice.

RESULTS OF TESTS

Hemolysis Tests.—A total of ninety-one hemolysis tests on fifty-four different babies were performed, fifty-two being with mother's serum and thirty-nine with cord serum (table 1).

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51. Ravdin, E. G.: An Estimation of the Clinical Value of the van den Bergh Test, Am. J. M. Sc. **169**:850, 1925.

52. Jones, B. B.: Isoagglutinins in the Blood of the New Born, Am. J. Dis. Child. **22**:586 (Dec.) 1921.

TABLE 1.—*Results of Ninety-One Hemolysis Tests on Infants*

Case	Hemolysis Tests: Mother Serum—Infants Cells							Cord Serum—Infant Cells							Degree of Jaundice: Day of Test	Degree of Jaundice: Maximum	Van den Bergh Test	Fragility	Group: Infant	Group: Mother
	1:2	1:4	1:8	1:16	1:32	1:34	C	1:2	1:4	1:8	1:16	1:32	1:64	C						
B-4	100	75	50	25	T	0	0	..	...	...	...	...	...	...	+++	++++	16.3	0.425-0.275	I	IV
C-4	0	0	0	0	0	0	0	25	0	0	0	0	0	0	+++	++++	17.2	0.400-0.300	II	II
C-42	0	0	0	0	0	0	0	T	T	T	T	T	T	0	+++	++++	14.0	.....	III	III
L-4	25	T	0	0	0	0	0	50	25	25	T	0	0	0	++++	++++	17.5	.....	II	II
R-4	0	0	0	0	0	0	0	..	...	...	...	...	...	...	++	++++	14.0	.....	II	II
U-4	25	10	10	T	T	0	0	..	...	...	...	...	...	...	+++	++++	....	.....	III	III
W-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+++	++++	....	0.400-0.300	IV	IV
B-3	T	T	0	0	0	0	0	..	...	...	...	...	...	...	+++	+++	....	.....	I	I
D-3	50	T	0	0	0	0	0	..	...	...	...	...	...	...	+	+++	18.8	.....	III	III
H-3	0	0	0	0	0	0	0	25	T	T	0	0	0	0	++	+++	18.0	0.425-0.275	I	I
H-32	0	0	0	0	0	0	0	0	0	0	0	0	0	0	++	+++	....	.....	IV	III
K-3	100	100	100	100	0	0	0	..	...	...	...	...	...	...	++	+++	5.3	.....	IV	IV
M-3	100	90	T	0	0	0	0	0	0	0	0	0	0	0	+++	+++	....	.....	II	II
M-32	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+++	+++	....	.....	0	II
M-33	T	T	0	0	0	0	0	0	0	0	0	0	0	0	+	+++	....	0.550-0.325	I	I
P-3	0	0	0	0	0	0	0	..	...	...	...	...	...	...	0	+++	....	.....	I	
R-3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+++	+++	....	.....	I	I
S-3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	++	+++	....	.....	0	I
W-3	50	25	10	10	T	T	0	..	...	...	...	...	...	...	+	+++	....	.....	II	II
Z-3	25	25	T	0	0	0	0	0	0	0	0	0	0	0	+++	+++	15.8	0.400-0.250	II	IV
B-1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	++	++	....	0.400-0.325	0	II
C-1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	+	++	....	.....	II	IV
C-12	0	0	0	0	0	0	0	..	...	...	...	...	...	...	0	+	7.6	.....	II	II
H-1	T	0	0	0	0	0	0	0	0	0	0	0	0	0	+	++	....	.....	0	III

H-12	0	0	0	0	0	0	0	..	...	...	...	...	...	...	+	++	....	.....	III	IV
K-1	T	T	T	T	0	0	0	0	0	0	0	0	0	0	++	++	5.3	.....	II	II
M-1	T	T	T	T	T	T	0	0	0	0	0	0	0	0	0	++	....	.....	0	IV
M-12	10	T	T	T	T	T	0	0	0	0	0	0	0	0	++	++	....	.....	III	III
M-13	T	T	0	0	0	0	0	0	0	0	0	0	0	0	+	+	4.2	.....	0	IV
M-14	75	50	T	0	0	0	0	..	...	...	...	...	...	...	++	++	....	.....	II	II
S-1	50	T	0	0	0	0	0	..	...	...	...	...	...	...	++	++	....	.....	0	III
S-12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	++	++	12.4	0.400-0.275	II	II
S-13	10	10	T	T	T	0	0	0	0	0	0	0	0	0	++	++	12.6	.....	II	III
W-1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	++	++	....	0.375-0.325	IV	IV
A-0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	....	.....	III	IV
B-0	90	10	T	0	0	0	0	0	0	0	0	0	0	0	0	0	6.0	.....	II	II
C-0	T	T	T	T	T	0	0	T	T	T	T	T	T	0	0	0	1.6	.....	IV	IV
C-02	0	0	0	0	0	0	0	..	...	...	...	...	...	...	0	0	....	.....	II	IV
F-0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	....	0.525-0.250	III	III
F-02	0	0	0	0	0	0	0	0	0	0		0	0	0	0	0	....	0.400-0.250	0	IV
G-0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	....	.....	0	IV
G-02	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	....	.....	II	II
G-03	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3 5	.....	I	III
H-0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	7.6	.....	0	II
K-0	T	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	8.0	0.425-0.275	II	II
L-0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	....	0.375-0.325	II	II
M-0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1.0	.....	II	II
M-02	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	....	.....	III	IV
N-0	0	0	0	0	0	0	0	25	T	0	0	0	0	0	0	0	1.0	0.425-0.300	IV	IV
O-0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2.0	.....	0	IV
P-0	0	0	0	0	0	0	0	..	...	...	...	...	...	...	0	0	1.8	.....	II	II
R-0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1.3	0.400-0.300	0	II
S-0	0	0	0	0	0	0	0	0	0	0	0	0	0	9	0	0	....	.....	IV	III
W-0	0	0	0	0	0	0	0	..	...	...	...	...	...	...	0	0	....	.....	0	IV

In the fifty-two cases in which mother's serum was used, hemolysis of the infant's cells occurred in nineteen, of which number seventeen were infants with jaundice (table 2). Of thirty-three babies with jaundice, seventeen or 51 per cent showed hemolysis. Thus it is demonstrated that there is present in the serum of the mother a substance capable of hemolyzing the red blood cells of her infant in vitro and that in 90 per cent of the cases in which hemolysis occurred, the infants showed clinical jaundice. This substance is also present in cord serum but in lower titer, as would be expected.

The fact that hemolysis occurred in a few babies who were not jaundiced does not in itself militate against the hemolysin so demonstrated being a specific factor in the production of jaundice of the newborn. It is generally conceded and on good grounds that the line between infants with and those without jaundice is not a sharp one; that the process is one active in every baby and that the presence or absence of clinical jaundice is purely an expression of its degree. It is not strange, then, that in an occasional case not showing clinical jaun-

TABLE 2.—*Results of Hemolysis Tests in Mother's Serum and Cord Serum*

	Mother's Serum			Cord Serum		
	Total	Hemolysis	No Hemolysis	Total	Hemolysis	No Hemolysis
Total number of cases.....	52	19	33	39	7	32
Jaundice.....	33	17	16	23	5	18
No jaundice.....	19	2	17	16	2	14

dice it is possible to demonstrate hemolysis in vitro by the mother's serum. A more detailed analysis of the tests shows further (table 1) that of the four tests showing hemolysis in nonjaundiced infants, two were made on the same infant and that this baby, although it did not show clinical jaundice had a van den Bergh reaction of 6 units; one of the other two gave a reaction of 8 units, which is well above the average of 4 units given by babies without jaundice. So while there was no demonstrable clinical evidence of jaundice in these cases, two of the three babies gave laboratory evidence of jaundice comparable in degree to that of mildly jaundiced babies, whose average van den Bergh reading was 8.7 units.

In five cases with jaundice in which the infant's serum was set up against his own cells, autolysins were not demonstrated. In one case in which the serum of a mother hemolyzed the cells of her jaundiced baby, her serum also hemolyzed the cells of a baby without jaundice and of the same blood group. This baby's cells were not hemolyzed by his own mother's serum. The serum of three mothers with babies without jaundice, failed to hemolyze the cells of jaundiced babies of the same group which were hemolyzed by the serum of their own mothers.

Van Den Bergh Tests.—The van den Bergh test was performed with the object of adding data to those already published on the type of reaction obtained in jaundice of the new-born infant, no large series using

TABLE 3.—*Results of van den Bergh Tests*

Case	Van den Bergh		Age in Days	Degree of Jaundice	
	Cord Blood	Infant's Blood		Day of Test	Maximum
B-4	...	17.4	10	++++	++++
B-42	...	16.3	6	++++	++++
C-4	...	17.2	3	++++	++++
L-4	1.6	17.5	5	++++	++++
L-42	...	26.0	6	++++	++++
M-3	...	28.5	7	++++	++++
S-4	...	18.8	10	++++	++++
Average	1.6	20.2	7		
C-42	...	14.0	3	+++	++++
D-3	...	18.8	6	+++	++++
H-3	1.5	18.0	3	+++	+++
H-32	...	20.0	5	+++	+++
H-33	2.0	....	..	.....	+++
H-34	...	15.0	7	+++	+++
M-32	3.3	14.0	10	+++	+++
R-4	...	15.0	7	+++	++++
T-3	4.2	....	..	.....	+++
Z-3	1.5	15.8	3	+++	+++
Average	2.2	16.6	5		
B-2	...	12.0	3	++	++
C-2	...	7.6	6	++	++
J-2	...	16.4	6	++	++
K-2	...	5.3	9	+	++
M-2	1.0	4.2	3	+	++
S-2	1.9	12.4	3	++	++
S-22	...	12.6	9	++	++
T-2	...	12.0	12	++	+++
M-4	...	7.2	7	++	++++
K-3	...	5.3	15	+	+++
L-3	...	1.0	8	++	+++
Average	1.45	8.7	7		
A-1	1.0	1.1	5	0	0
A-12	3.3	....	..	0	0
B-1	...	6.0	3	0	0
C-1	...	1.6	8	0	0
G-1	...	12.0	7	0	+
F-1	1.5	....	..	0	0
F-12	1.5	....	..	0	0
G-12	2.4	3.5	5	0	0
H-1	...	7.6	7	0	0
K-1	2.1	8.0	6	0	0
M-1	...	1.0	9	0	0
M-12	...	0.6	7	0	0
N-1	...	1.0	8	0	0
O-1	1.1	2.0	5	0	0
P-1	...	1.8	5	0	0
R-1	...	1.3	7	0	0
S-1	...	9.5	6	0	0
T-1	...	1.8	7	0	0
T-12	...	1.2	10	0	0
W-1	...	8.0	4	0	0
Average	1.8	4.0	6		
General average	2.0	7.8	6.5		

infant's serum having been found in the literature. The direct reaction was not obtained in a total of fifty-eight cases, of which forty-three tests were made on blood obtained from the infant and fifteen on cord blood (table 3). In every case but one, the indirect reading

was distinctly above the adult normal (0.2 to 0.6 units). The cord serum was always above normal, 2 units, and not in any case in which first the cord blood and subsequently the infant's blood was tested did the latter fail to show the higher reading, thus indicating that the process is one started before birth and continued after it.

Yllpö [19] said that in general the van den Bergh test on the cord blood is higher in babies who later become jaundiced than in those who do not. In the small series here presented, it would not seem possible to make any predictions as to the later development of jaundice on this basis; although the jaundiced babies do show a slightly higher average for cord blood, 2.1 against 1.8. Turolt and Teyner report a series of twenty-five cases in which the general average for babies not developing jaundice is 2.15 against 1.94 for those who do.

The indirect van den Bergh reading checked well with the clinically estimated intensity of jaundice, although there were individual cases in which there was considerable variation.

Both incidence and intensity of jaundice is generally accepted as greater among premature than among full term infants. In the present series, three of a total of twelve premature babies were recorded clinically as not jaundiced. Two of these three babies died, and the van den Bergh tests were performed on blood drawn from their hearts immediately after death. The readings in these two cases at 10 and 7 days of age, respectively, were 1.8 and 1.2 units. The fact that two of these three babies died is interesting in view of Greil's statement that failure of a premature infant to develop intense and early icterus indicates a bad prognosis.

Van den Bergh tests were made on the blood of three mothers which was collected a few hours after delivery, and in two of these on the cord blood. The results were as follows: mother's blood: (1) 0.2, (2) 0.2, (3) 1.7; cord blood: (1) 3.3, (2) 1.9.

Fragility Tests.—There was no increased fragility of the red blood cells in the cases which showed hemolysis (table 1). Fragility was within normal limits in all but two of the fifteen cases in which it was tested. In these two cases (table 1 M33 and F1), hemolysis started at 0.550 and 0.525, respectively, and was complete at 0.325 and 0.250.

Blood Groups.—Blood group determinations were made on 141 newborn infants.[54]

Eighty-six of this group were jaundiced, and the blood group was formed at birth in 61 per cent, against 56 per cent for the remainder without jaundice (table 4). It is evident that the infants whose blood group was not formed at birth were not identical with those who became jaundiced.

54. The result of these blood groupings as they pertain to the time of formation of the blood group are to be reported separately.

Difference in the blood group of mother and infant was not a factor in the cases in which hemolysis was present, nor was there any relation between it and the presence of jaundice (table 1).

Incidence and Intensity.—There is great variation in the figures of different writers on the incidence of jaundice, but the majority fall between 60 and 80 per cent. Of 141 cases in the present series, 86 or 61 per cent were recorded as showing clinical jaundice. Of these, 14 per cent were markedly, 29 per cent moderately and 57 per cent slightly jaundiced. This division checks well with the intensity of jaundice as indicated by the indirect van den Bergh reading.

COMMENT

No attempt has been made to discuss all the various theories of the etiology of jaundice. An excellent review of those now given credence will be found by van Creveld.[55] The work of numerous investigators bearing on the hematogenous origin have been reviewed.

TABLE 4.—*Blood Group and Jaundice*

		Group Formed at Birth, in per Cent	Group Not Formed at Birth, in per Cent
Total Cases	141	59	41
Jaundice	86	61	39
No jaundice	55	56	44

Certain facts emerge from work of previous observers verified beyond question; others' contentions are challenged. We may not accept the van den Bergh test as proof conclusive of a hematogenous origin of jaundice, but it is corroborative evidence. Certainly there is some difference between the bilirubin of icterus neonatorum and that of obstructive jaundice.

The amount of bilirubin in the cord blood is greater than normal in all cases, greater than in the mother in most cases. Therefore, the process giving rise to jaundice has started before birth. This rules out birth hemorrhage and infection as essential and primary factors.[56] The amount of bilirubin increases rapidly after delivery, reaches a maximum and falls to normal in a time similar to that of clinical jaundice. Therefore, although the process starts in utero, it continues in an accelerated fashion, or else its products are not so well handled after delivery. This rise in bilirubin occurs in all cases, but its amount parallels the intensity

55. Van Creveld, S.: Icterus Neonatorum, Am. J. Dis. Child. **30**:240 (Aug.) 1925.

56. Further evidence of this is presented by the fact that in the present series two babies delivered by cesarean section prior to engagement of the head, subsequently became jaundiced.

of jaundice. Therefore the presence of clinical jaundice is merely an expression of the degree to which the process attains.

Iron, like bilirubin, having its origin in hemoglobin, is present in considerable quantities in the placenta, but almost absent in its storehouses (liver, spleen, tissues) in the fetus at the time of delivery. Iron increases rapidly in the liver and spleen after delivery, reaches a maximum and decreases in from five to six months to normal. All of these observations on iron and bilirubin hold alike for full term and premature infants, with the exception that there is a greater amount of iron in the placenta and in the liver in premature infants.

Decrease in the red blood count and hemoglobin of new-born infants concomitant with the appearance of jaundice is not proved. Unusual productivity of the hemopoietic system just subsequent to birth is known to occur. Injections of laked blood will produce jaundice even in the absence of the liver.

The mother's serum is capable of hemolyzing the red blood cells of the infant in a certain proportion of cases. Autolysins have been demonstrated. They are transitory.

In the present work, evidence is adduced that the mother's serum is capable of hemolyzing the red blood cells of her infant in 51 per cent of thirty-three icteric babies, 90 per cent of all cases that show hemolysis occurring in infants with clinical jaundice. The fact that hemolysis occurred in two nonjaundiced infants concurs with the fact that all babies show an increase in bilirubin after delivery, but that this rise corresponds with the clinically judged intensity of jaundice. Cord serum also possesses the property of hemolyzing infants' red blood cells but in a smaller proportion of cases and in lower titer, as would be expected.

Increased fragility of the red blood cells so far as can be judged by the use of hypotonic salt solution is not a factor.

Several questions are pertinent. If the process giving rise to jaundice is active in utero, why are babies not born jaundiced? What is the explanation of the sudden increase after delivery? Why is jaundice more common in the premature infant?

In the light of the present knowledge, a logical answer to these questions would seem to be that the process is active in utero, but that during this time the placenta is acting as an organ of excretion or of storage for the products of hemolysis, as is shown by its high iron content. At delivery, the placenta ceases to function, the process continues, products of hemolysis in the blood stream rise, giving evidence of their presence in jaundice, which fades as they are stored in the liver and other organs as iron, or are excreted. There may be then merely an apparent increase after delivery or there may be an actual increase on the hypothesis that the hemolysin in question acts like a cold agglutinin, the temperature of

the infant's body being lower following delivery than in utero; that jaundice may be more common in premature infants because at this time of development hemolysis is occurring at a higher rate, as is evidenced by the greater amount of iron in the placenta as well as in the liver, or because these weaker babies are less readily able to handle its products.

The author's conception of jaundice of the new-born infant is that it is an expression of hemolysis brought about by substances passing from the serum of the mother through the placenta, which is active in all infants in utero and after delivery.

Corroboration of the results of hemolysis tests here presented is awaited. Evidence of quantitative relation between the amount of blood destruction and increase in bilirubin is lacking. Reports in the literature and in this series on the bilirubin content of the blood of premature infants at birth are insufficient to show positively the relative amount of blood destruction going on at this time.

CONCLUSIONS

1. The blood serum of the mother contains a substance capable of hemolyzing the red blood cells of her infant in vitro. This substance is demonstrated in 51 per cent of thirty-three infants with jaundice. It is also demonstrated in lower titer in the cord blood in 22 per cent of twenty-three infants with jaundice.

2. All cord serums show an indirect van den Bergh reaction higher than normal. The direct van den Bergh reaction is not present in cord serums.

3. The serums of all infants under fourteen days of age show an indirect van den Bergh reaction higher than normal and higher than that of the cord serums. The reading parallels the intensity of jaundice. The direct reaction is not present in simple icterus neonatorum.

4. Increased fragility of the red blood cells is not a factor in the production of jaundice, nor in cases showing hemolysis by the mother's serum.

5. The time of formation of the blood group in new-born infants does not bear any relation to jaundice.

DIABETES MELLITUS IN CHILDREN

STUDIES OF THE HEIGHT AND WEIGHT OF FORTY-FIVE PATIENTS *

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Prior to the introduction of insulin, diabetes mellitus in children ran a rapidly progressive course, often proving fatal within six months after the symptoms had become sufficient to lead to a correct diagnosis. With rigid dietetic treatment and intelligent care, it was occasionally possible to prolong the life of the older children for two or three years. However, the diet on which life was sustained was inadequate for normal growth and development in these children. Consequently, the typical diabetic child on dietetic treatment in the preinsulin days was much undernourished and stunted in growth, if the mildness of his disease permitted his survival.

Insulin has revolutionized the treatment of diabetes in patients of every age, but the most striking and encouraging results have been obtained in the treatment of the disease in children. Now it is possible to supply the immediate metabolic requirements of these children so that they not only live, but live well on diets closely approaching those of normal children. However, a therapy should not be accepted as a completely achieved ideal form of treatment for children, no matter how great may be its advantages over methods previously in use, unless it restores their normal rate of growth and development.

It was felt that it would be of interest to determine whether or not diabetic children were of normal stature at the time of the onset of their symptoms, as it has been suggested that diabetes may not be a disease of the pancreas alone, but that it may also involve some of the other glands of internal secretion and consequently affect the growth and development of children even before definite manifestations of a disturbed carbohydrate metabolism become evident.

It was also felt that it was desirable to determine the rate of growth of diabetic children at this clinic while they were receiving treatment with insulin which, although apparently adequate for their immediate metabolic needs, might not be sufficient to counteract the definitely retarding influence which this disease has on growth and development when the patients are treated by dietary regimen alone. A similar study has been made by Joslin and others,[1] but data on the growth and develop-

* Received for publication, May 17, 1928.

* From the Infants' and Children's Hospital and the Department of Pediatrics, Harvard Medical School.

1. Joslin, E. P.: End-Results in the Treatment of Diabetes Mellitus in Children, J. A. M. A. **88**:28 (Jan. 1) 1927.

ment of diabetic children is strikingly infrequent in medical literature, so it was believed that it would be of interest to record the results of the analysis of this series of patients.

The records of the diabetic children under 13 years of age who have been treated at the Infants' and Children's Hospital during the last five years have been reviewed. The records retained for analysis were only those of patients with proved diabetes mellitus who had sought treatment at this clinic within six months after the onset of diabetic symptoms, and who had measurements recorded of their weight and height when they first came under observation. In addition to the series of twenty-three patients from this clinic, a group of twenty-two similar cases were selected by the same criteria from among those reported by Allen and Sherrill,[2] and a corrsponding analysis of both series was made.

TABLE 1.—*Actual Height and Weight Compared with Average Normal for Age* *

	Height	Weight
23 patients from Infants' and Children's Hospital		
Above normal	11	2
Normal	6	10
Below normal	6	11
22 patients of Allen and Sherrill		
Above normal	15	3
Normal	4	10
Below normal	3	9
45 patients—Combined Series		
Above normal	26	5
Normal	10	20
Below normal	9	20

* In this table and table 2, the normal weight is ± 10 per cent of average normal weight and the normal height, ± 1 inch of average normal height.

The normal standards used for comparison were the tables in Griffith and Mitchell's textbook on the "Diseases of Infants and Children." These tables are the familiar ones of Bowditch, Heuber, Wood and the Children's Bureau, which represent the average normal height and weight of children of both sexes at the ages under consideration.

The normal variation in weight was considered to lie within a range of plus or minus 10 per cent of the weight given in the tables, and normal height was arbitrarily chosen to vary within 1 inch of that given in the tables for the stated age (tables 1 and 2). However, in order that the results of the analysis might be more directly comparable with those of Joslin, Root and White,[3] the records were also

2. Allen, F. M., and Sherrill, J. W.: Clinical Observations with Insulin, J. Metab. Research **2**:803 (Nov.-Dec.) 1922.

3. Joslin, E. P.; Root, H., and White, P.: Growth, Development and Prognosis of Diabetic Children, J. A. M. A. **85**:420 (Aug. 8) 1925. White, Priscilla: The Potential Diabetic Child, J. A. M. A. **88**:170 (Jan. 15) 1927.

reviewed, a zone of normal deviation from the average weight as stated in the tables not being allowed for, and a variation from the average height of only 1/8 inch being permitted, which was considered to be the limit of accuracy in obtaining the measurement (tables 3 and 4).

In ten patients being treated with insulin, who had been under observation for a sufficient length of time, the rate of growth determined by their gain in weight and increase in stature was compared with that

TABLE 2.—*Actual Weight Compared with Expected Weight for Average Height and for Actual Height*

	Average Height	Actual Height
23 patients from Infants' and Children's Hospital		
Above normal	2	1
Normal	9	6
Below normal	12	16
22 patients of Allen and Sherrill		
Above normal	3	1
Normal	7	6
Below normal	12	15
45 patients—Combined Series		
Above normal	5	2
Normal	16	12
Below normal	24	31

TABLE 3.—*Actual Height and Weight Compared with Average Normal for Age**

	Height	Weight
23 patients from Infants' and Children's Hospital		
Above normal	14	4
Normal	2	1
Below normal	7	18
22 patients of Allen and Sherrill		
Above normal	18	5
Normal	1	0
Below normal	3	17
45 patients—Combined Series		
Above normal	32	9
Normal	3	1
Below normal	10	35

* In this table and table 4, the normal weight is the average normal and the normal height, ± 1/8 inch of average normal.

of the average normal child of corresponding age during the same interval of time. Observations were also tabulated, showing the sex, age incidence, presence of diabetes in other members of the family, season of onset and duration of symptoms before medical advice was sought. The "best" or maximum weight had not been reported in a sufficient number of cases to be of value in the analysis, although in many patients recent loss of weight was among the outstanding symptoms. Consequently, it was not possible to determine whether these children had been considerably overweight before the development of diabetic symptoms, as is so frequently the case among adult patients.

Analysis of tables 1 and 2 shows that of 45 patients 36 (80 per cent) were of normal height or above for their age; 26 (59 per cent) were 1 or more inches overheight for their age; 9 (20 per cent) were 1 or more inches underheight for their age; 20 (44 per cent) were more than 10 per cent underweight for their age, and 31 (69 per cent) were more than 10 per cent underweight for their actual height.

Analysis of tables 3 and 4 without a zone of normal deviation in height and weight shows that of 45 patients 35 (78 per cent) were of normal height or above for their age; 32 (71 per cent) were overheight for their age; 10 (22 per cent) were underheight for their age; 35 (78 per cent) were underweight for their age, and 34 (75 per cent) were underweight for their actual height.

The predominance of excess height among these children is in accordance with the observations reported by White.

TABLE 4.—*Actual Weight Compared with Expected Weight for Average Height and for Actual Height*

	Average Height	Actual Height
23 patients from Infants' and Children's Hospital		
Above normal	4	3
Normal	0	0
Below normal	19	20
22 patients of Allen and Sherrill		
Above normal	4	5
Normal	0	3
Below normal	18	14
45 patients—Combined Series		
Above normal	8	8
Normal	0	0
Below normal	37	37

Of fifty-three patients whose sex was noted but of whom eight lacked physical measurements requisite for their inclusion in the group of patients selected for more complete analysis, there were twenty-four males and twenty-nine females. In twenty-seven patients the onset of symptoms of diabetes occurred before they were 6 years old and in twenty-six the symptoms developed after that age.

Of thirty-one patients in whom the duration of symptoms before medical advice was sought could be accurately determined by their history, sixteen, or 52 per cent, had symptoms of less than one month's duration, demonstrating the often noted acute type of onset of diabetes in childhood. However, the remarkable improvement in prognosis since the introduction of insulin is shown by the fact that there has not been a single death among the diabetic children treated at the Infants' and Children's Hospital during the last five years.

In five, or 16 per cent, of the children, it was noted that diabetes was also present among the siblings, parents or aunts and uncles. Seasonal incidence showed that nineteen patients, or 61 per cent, devel-

oped symptoms of the onset of diabetes between April and September, whereas in only twelve, or 39 per cent, the onset occurred between October and March. This suggests that the greater general incidence of acute respiratory infections occurring during the winter months is not an important factor in precipitating the onset of diabetic symptoms in the majority of the patients. This appears contrary to the observations of Adams [4] and Boyd.[5]

In addition, ten children have been studied who were under observation in the regular diabetic clinic of the outpatient department for an average period of 2.2 years immediately after the recognition of the disease, in order to detect any variations from the average normal rate of growth in height and gain in weight. They were given diets considered adequate for the needs of normal growth and sufficient insulin to keep their urine free from sugar as much of the time as possible without producing evidence of hypoglycemia. However, during the period of observation the ten diabetic children showed an average growth in height of 3.8 inches (9.6 cm.), or 76 per cent of the average normal growth of 4.97 inches (12.3 cm.) for children of identical ages and during the same periods of observation. The average gain in weight of the diabetic children was 10.07 pounds (5.3 Kg.), or 76 per cent of the average normal gain of 13.17 pounds (6.6 Kg.) during the same period. Thus, both growth in height and gain in weight of diabetic children during the first two years under insulin treatment was 24 per cent below normal. This is all the more striking because of the fact that it has been shown that up to the time of onset of the disease these children had grown in height more than the average normal child.

The failure of diabetic children to grow at the normal rate, even when treated with insulin, may be due in part to the fact that great difficulty was experienced in obtaining the desired amount of intelligent care and helpful cooperation among the type of patients generally attending the clinic of the outpatient department, for it is recognized that the results obtained in the treatment of persons with diabetes are greatly influenced by the ability of those having the immediate daily care of the patient at home to follow the instructions of the physician and to use their own intelligent initiative as they gain familiarity with the principles involved in the modern treatment of patients with diabetes.

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4. Adams, S. F.: Seasonal Variations in Onset of Acute Diabetes, Arch. Int. Med. **37**:861 (June) 1926.

5. Boyd, G. W.: Diabetes in Children, Arch. Pediat. **41**:291, 1924; Treatment of Diabetes in Children, Am. J. Dis. Child. **29**:329 (March) 1925; Course and Prognosis of Diabetes in Children, Tr. Canad. Soc. for Study of Dis. of Child., 1927, Am. J. Dis. Child. **34**:698 (Oct.) 1927.

CONCLUSIONS

1. Analysis of the record of 45 diabetic children shows that at the onset of the disease, 36 (80 per cent) were of normal height or above for their age; 26 (59 per cent) were at least 1 inch above normal height for their age; 20 (44 per cent) were more than 10 per cent underweight for their age, and 31 (69 per cent) were more than 10 per cent underweight for their height. The typical diabetic child at the time of onset of the symptoms of the disease is tall and slender (overheight for age and underweight for both age and height).

2. Ten diabetic children under observation for an average period of 2.2 years following the onset of their disease, while receiving treatment with insulin, showed a rate of gain in height and in weight of 24 per cent below the normal rate. This decrease in the rate of growth in height after the onset of diabetes is all the more striking since it has been shown that prior to developing the disease these children had grown in height more than the average normal child.

3. Improvement in prognosis among the juvenile patients since the introduction of insulin is demonstrated by the fact that there has not been a single death among the diabetic patients treated at the Infants' and Children's Hospital during the last five years.

4. The incidence of sex, age, duration of symptoms, season of onset and presence of diabetes in other members of the family were also noted.

Case Reports

ACTINOMYCOSIS OF THE LUNG

REPORT OF A CASE IN WHICH BRONCHOSCOPY AND INJECTIONS OF IODIZED OIL 40 PER CENT WERE USED *

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AND
JOHN DEVEREUX KERNAN, M.D.
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History.—This patient, a boy, came under observation, Dec. 27, 1922, at the age of 6 weeks. At birth he weighed 6½ pounds (2,954 Gm.) and never reached standard height or weight for his age. Except for tonsillitis at 14 months, he enjoyed good health until the present illness. In the summer of 1925, he lived on a farm in Iowa and developed a habit of chewing grass.

In October, 1925, at the age of 3 years, he began to cough. This continued all winter but was not thought serious enough to require medical advice. In June, 1926, however, he began to lose weight and to have a slight elevation in temperature. He was then brought to the hospital for examination. Over the base of the right lung, marked dulness with amphoric breathing was found. A diagnosis of abscess of the lung was suggested, although history of the inhalation of a foreign body was not obtainable. Clubbing of the fingers and toes was present. A roentgen-ray examination showed a shadow in the lower lobe of the right lung which was interpreted as consolidation (fig. 1). Intracutaneous tests and examinations of the sputum were negative for tuberculosis.

The blood count on June 22 showed: hemoglobin, 40 per cent; red blood cells, 2,720,000; white blood cells, 31,000 with 87 per cent polymorphonuclear leukocytes.

On June 22, 1926, one of us (J. D. K.) passed a bronchoscope. Just below the opening of the bronchus of the middle lobe, there was an edematous swelling of the mucous membrane. Beyond this point, what seemed like a foreign body was seen. This was coughed up, and immediately afterward a large amount of foul-smelling pus was released and aspirated. This object proved to be a piece of fibrin. The breath became foul after the bronchoscopy.

For three weeks following the operation, the shadow on the lung became less dense, and the general condition improved (fig. 2). The improvement, however, did not continue and another bronchoscopy was done on July 30. Although bronchoscopies were repeated eight times during September, October and November, the process extended into the upper and middle lobes of the right lung, and the child's general condition grew worse (fig. 3). At this time the organism of actinomycosis was isolated.

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* Read before the Section of Pediatrics, New York Academy of Medicine, April 12, 1928.

* From the Babies' Hospital, the Department of Diseases of Children, College of Physicians and Surgeons.

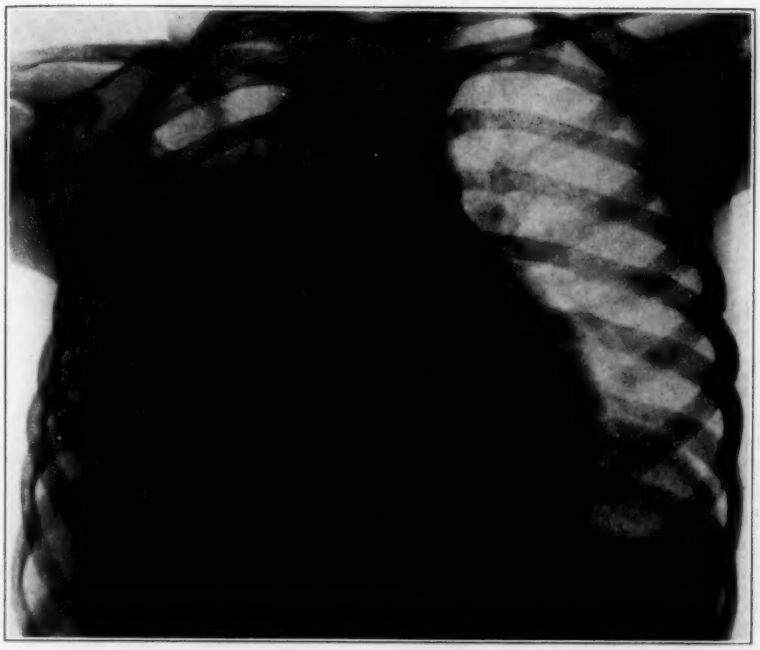

Fig. 1.—Roentgenogram taken on June 22, 1926, showng the lesion worst in the lower lobe of the right lung.

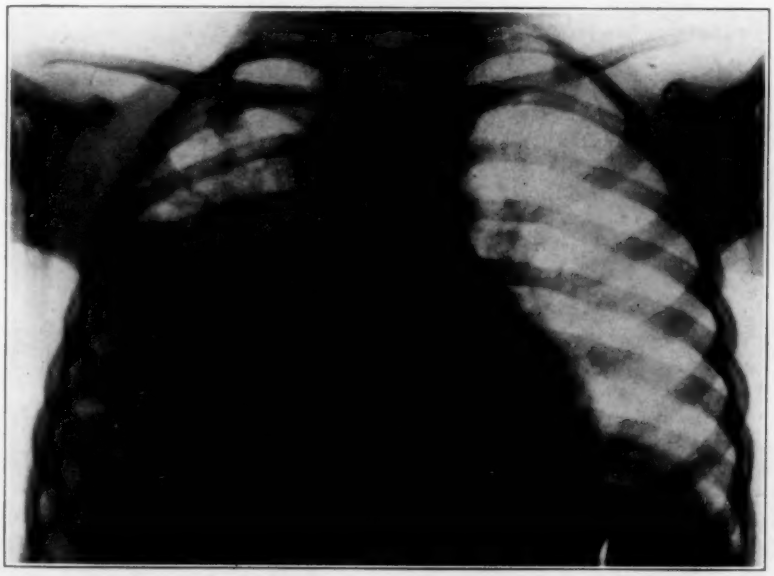

Fig. 2.—Roentgenogram taken on July 3, 1926, showing improvement after the first bronchoscopy.

From December to March, seven more bronchoscopies were done, and at each one, 5 cc. of iodized oil 40 per cent was injected into the diseased lung. Large doses of potassium iodide, 60 grains (3.9 Gm.) a day, and deep roentgen-ray therapy were also given. During the entire illness, postural drainage was encouraged. At each bronchoscopy, small amounts of sanguineous purulent material were aspirated. The amount drained or aspirated was never sufficient to empty the cavities. The material in the cavities as found at necropsy was too tenacious and thick to be aspirated through a bronchoscope.

From the time the administration of iodized oil was started, until the child developed pneumonia in March, 1927, there was a steady improvement in the weight and general condition (fig. 4). He died on March 8, 1927, of pneumonia.

Necropsy (Dr. Martha Wollstein).—The body was that of a fairly well nourished child. Lesions of the skin were not present. Examination of the head was not permitted.

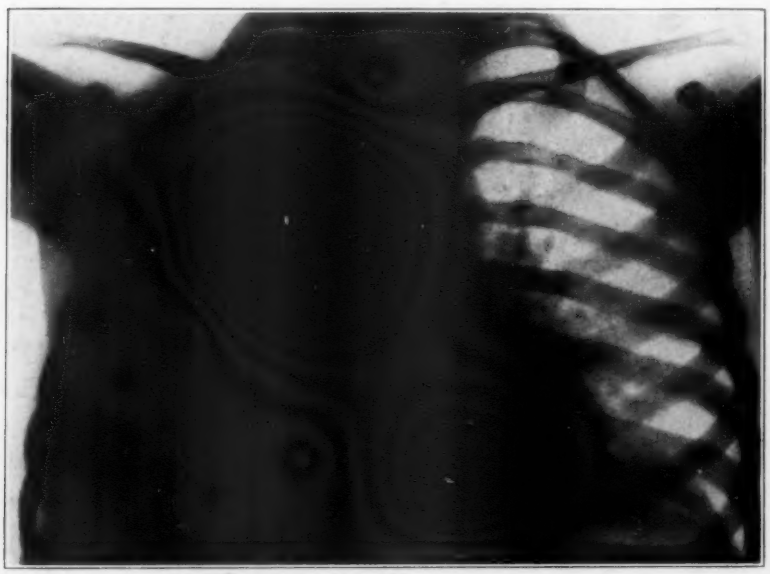

Fig. 3.—Roentgenogram taken on Sept. 4, 1926, showing the extension of the process throughout the right lung.

In the left lung, both the upper and the lower lobes were solid as a result of recent, red, conglomerate bronchopneumonia. Congestion and edema were intense. Over the lower lobe the pleura was dull, with a thin fibrinous exudate. The right lung was so adherent to the parietal pleura that the latter stripped from the ribs on removal. These adhesions were oldest and densest over the upper lobe. Fluctuation was present because a cavity, 10 by 6 by 5 cm., occupied most of the lower lobe, the posterior half of the middle lobe and the lower half of the upper lobe, and contained 36 Gm. of rounded masses of yellowish green, foul mucoid material. The walls were thinnest in the right middle lobe and at the apex of the lung. The lining was smooth, with the appearance of a pyogenic membrane. The cavity had three loculi, the largest in the lower lobe. In the posterior half of the right upper lobe, fibrosis had occurred, and contraction gave the appearance of a scar. In the apex of the lower lobe this condition was less marked.

The larynx and trachea showed a congested mucosa, but ulceration and thickening were not found. The left main bronchus and its branches were normal. The right main bronchus had a bright red mucosa and thickened walls, most marked in the branch going to the upper lobe, but present in all the bronchi in the right lung.

At the bifurcation of the trachea was a lymph node that was 3 cm. long by 2 cm. wide. It was soft, moist, congested and smooth on section. On the right main bronchus there was a node of similar size. On the left side, the nodes were only slightly enlarged.

Anatomic Diagnosis.—The condition was diagnosed as pulmonary cavitation, chronic pleurisy, pulmonary fibrosis, acute bronchopneumonia with fibrinous

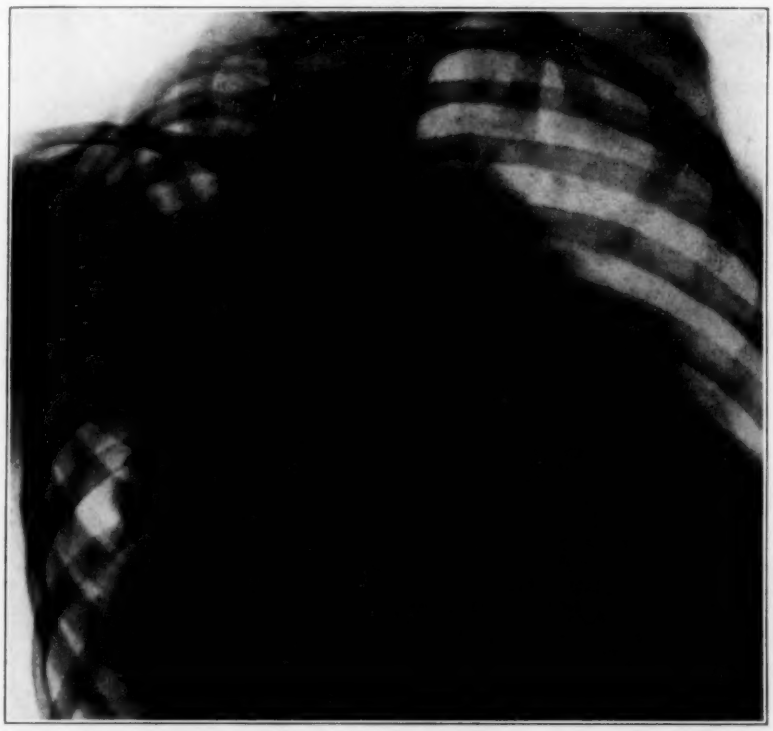

Fig. 4.—Roentgenogram taken on Feb. 4, 1927, after five injections of the iodized oil 40 per cent showing the iodized oil in the cavity and the marked improvement in the lung.

pleurisy, fatty liver and hyperplasia of the bronchial, mesenteric and intestinal lymph nodes.

Microscopic Examination.—Lung, Section 1: The interlobular septums of fibrous connective tissue were wide. The alveoli either were empty or contained large mononuclear phagocytic cells, some polymorphonuclear cells and some coagulated serum. Most of the alveolar walls were thickened. At the periphery of the lobules were alveoli lined with low epithelia, embryonal in type. The

bronchi had thickened walls and contained leukocytes and peeled epithelium. Some were compressed. Colonies of the ray fungus were not found.

Section 2: The pleura was thickened with a wide layer of granulation tissue and fibrous connective tissue. The septums were also thickened. Several arteries showed thickening of the intima. Normal lobules were not found in this section; many showed the alveolar walls in contact, and others were lined with low epithelial cells. There were a few lobules in which the alveoli contained fibrin as well as monocytes and polymorphonuclear cells. The bronchi contained polymorphonuclear cells in large numbers. Some had lost their epithelium. The wall of a cavity showed granulation tissue with loops of capillaries on the free surface, without lining epithelium. There were irregular areas of necrosis in the wall and masses of threads (mycelia) extending deeply into it. It is probable that the large amount of fibrosis in this section was the result of

Fig. 5.—The right lung opened to show the large cavity after the mucoid material was removed. This extended into all three lobes.

the roentgen-ray treatment. The inner wall of the cavity was folded as though it might have originated from a bronchus.

Section 3: There were large areas of fibrous connective tissue, while the lobules of the lung were small and compressed. The adventitia of all blood vessels was thickened, and some of the smaller vessels showed thickening of the intima as well. Several bronchi showed necrosis of the lining and thickening of the outer coat. The roentgen-ray treatment had undoubtedly modified the lesion. There was one small, round area which had the shape and size of a colony of *Actinomyces*, but the outline was blurred and threads could not be made out. Sections stained by Wright's method failed to show definite colonies of *Actinomyces*, though several places were suggestive of such colonies. The lesion throughout all these sections from the lungs was one of fibrosis and chronic inflammation of the bronchi, none of which were normal.

Left Lung: The pleura was edematous, but its covering cells were intact. Many alveoli contained serum, polymorphonuclear cells and peeled epithelia. The

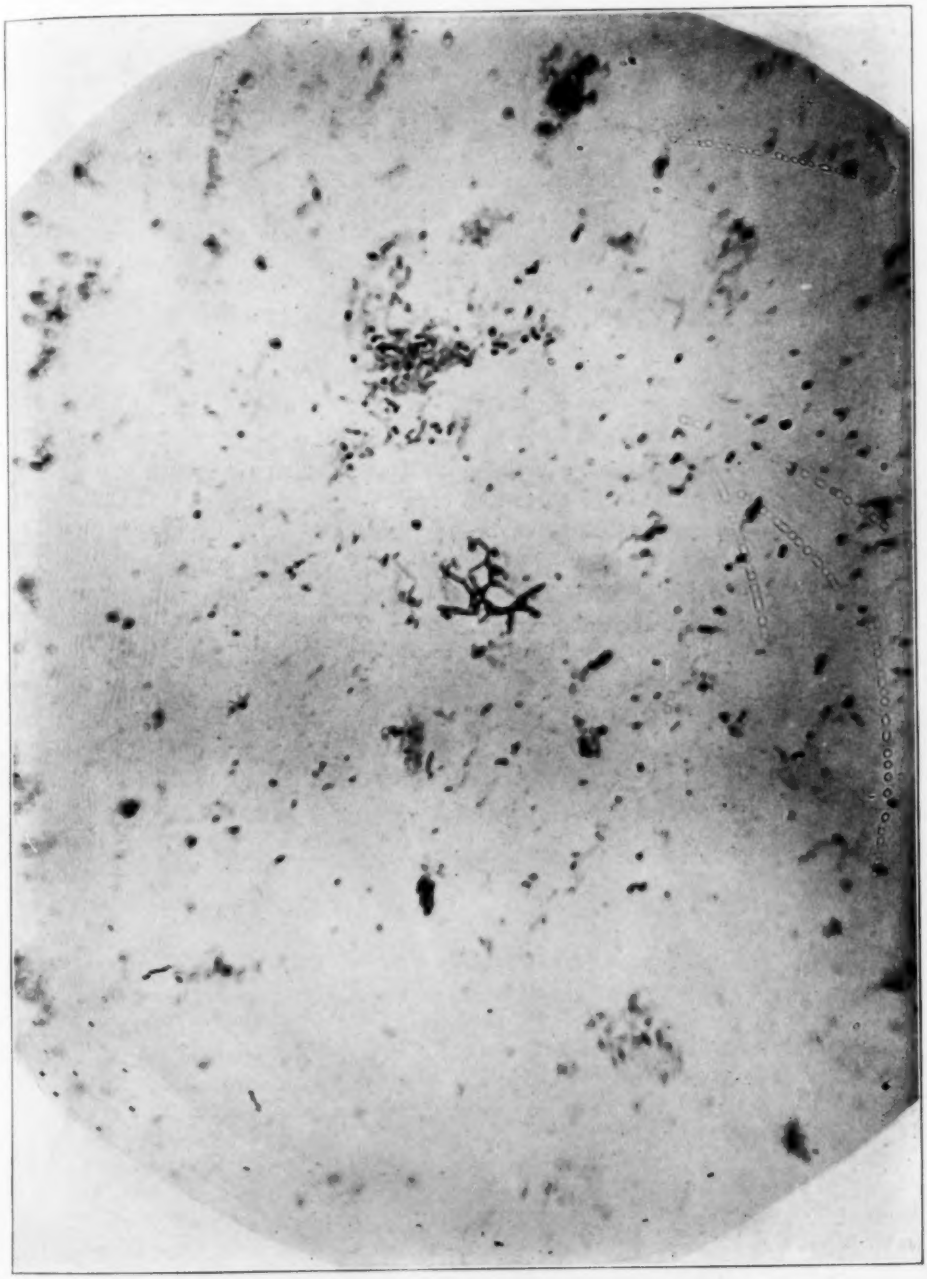

Fig. 6.—Cultures of organism of actinomycosis.

vessels were filled with red cells. The lesion in this lung was caused by edema and early bronchopneumonia.

Actinomycotic nodules were not found in any of the other organs.

Bacteriologic Examination.—In spreads from thick mucoid material obtained by one of us (J. D. K.) on bronchoscopic examination, short branching threads with clubbed ends were found, which stained with methylene blue and retained the Gram stain. They were not acid fast. In anaerobic glucose-agar cultures colonies of actinomyces developed, but the growth was not pure. Broth cultures grew with round, gray masses falling to the bottom of the flasks.

Subcutaneous, intravenous and intraperitoneal inoculations into guinea-pigs and rabbits gave entirely negative results.

From the material obtained at necropsy, a growth of *Actinomyces* was obtained in broth cultures, but animal inoculations gave negative results.

COMMENT

This case is reported because of the rarity of the condition and because we believe that the injection of iodized oil 40 per cent by bronchoscopy offers a new method of treatment. This should be supplemented by large doses of potassium iodide by mouth.

This case proves that many bronchoscopies may be performed on a child aged 3 years without injury to the larynx, trachea or bronchus.

Actinomycosis should be suspected in all children with abscesses of the lung who have been playing on the ground in the country.

There may be great difficulty in growing the organism of actinomycosis as illustrated in this case.

MECKEL'S DIVERTICULUM WITH HEMORRHAGE *

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The literature on Meckel's diverticulum as a cause of intestinal hemorrhage was briefly reviewed by Abt and Strauss,[1] and three cases were reported. In the discussion of this paper, five additional cases were cited. The important feature in all but two of the foregoing cases was bleeding from the rectum. Ulceration of the mucosa of the diverticulum was usually the origin of the bleeding. In few of these cases was the diagnosis made before the operation. Because of the rarity of this condition, its relative seriousness and the necessity for immediate operation, this case is reported.

REPORT OF CASE

A boy, aged 6 years, was referred to the hospital because of bleeding from the rectum. Seven months previously, he had been bunted in the abdomen and knocked down by a cow. There had not been any evidence of injury. One month later, he had been struck in the right groin with the tongue of a wagon. There had been considerable pain, and a small hematoma had developed in the scrotum. The next day the child had complained of pain in the abdomen and had begun to vomit. He had been put to bed, and his symptoms had continued for two days. The physician who was called stated that he found the patient almost moribund and very pale, with a distended abdomen. Blood was not noted in the stools. The condition was diagnosed as acute appendicitis. The abdomen was opened and the peritoneal cavity found full of free blood. Because of the pallor and shock, exploration was not made. A drain was inserted and the abdomen closed. An uneventful recovery followed, and the boy was apparently well until two weeks before the present illness when he developed a "grip infection." He remained up and about. One week later dark clots of blood were noted in each daily stool. The day preceding admission to the hospital he passed two black, tarry stools, and the next morning approximately 3 ounces (89 cc.) of dark blood was passed on two occasions.

On admission to the Milwaukee Children's Hospital the boy was pale, listless and weak; the abdomen was scaphoid and not tender; petechiae were not present; dried blood could be seen around the anus. The urine was normal and remained so throughout the stay in the hospital without any blood being found. The blood count showed: erythrocytes, 3,280,000; hemoglobin, 35 per cent; leukocytes, 17,450, with 77 per cent neutrophils; 19 per cent small and 3 per cent large lymphocytes, and 1 per cent mononuclears; marked anisocytosis and poikilocytosis; platelets,

* Received for publication, April 17, 1928.
* From the Milwaukee Children's Hospital.
* Presented at the Chicago Pediatric Society, May 15, 1928.

1. Abt, Isaac A., and Strauss, Alfred: Meckel's Diverticulum as Cause of Intestinal Hemorrhage, J. A. M. A. **87**:91 (Sept. 25) 1926.

98,000. This and the results of subsequent examinations of the blood are shown in the accompanying table. The bleeding time was one minute and the coagulation time, three and one-half minutes. The blood group was IV (Moss). The rectal temperature was 100 F.; the pulse rate, 128 and respirations, 30. Two hundred cubic centimeters of citrated blood was transfused and the patient kept quiet and warm. The following day the condition was much improved, but slight epistaxis was present. The coagulation time with the Lee method was seven minutes; the calcium time, seventeen minutes; the plasma prothrombin time was normal, but there was no retractility of the clot in twenty-four hours. The stools were black

Data of Examinations of the Blood

Date	Event	Red Cells	Hemoglobin, per Cent (Dare)	White Cells	Neutrophils	Large Lymphocytes	Small Lymphocytes	Other Cells	Anisocytes Poikilocytes	Platelets
2/15	Admission	3,280,000	35	17,450	77	3	19	Mononuclear—1	Numerous	98,000
2/15	Transfusion									
2/16	.....	3,620,000	55	7,800	69	6	24	1	Numerous	
2/18	.....	.....	..	.....	..	..	..	..	..	a.m., 101,000 p.m., 150,000
2/19	40 cc. of blood intramuscularly	3,550,000	52	10,250	72	4	..	4	Few	
2/20	.....	.....	..	.....	..	..	..	..	..	98,000
2/22	Transfusion: 200 cc. whole blood citrated at 10 a.m.	2,120,000	55	.....	..	..	..	..	..	8 a.m., 92,000 11 a.m., 156,000 1:30 p.m., 140,000 3 p.m., 106,000 5 p.m., 110,000
2/23	.....	.....	..	.....	..	..	..	..	..	128,000
2/24	Before operation	3,840,000	55							
2/27	.....	3,800,000	50	14,450	..	..	..	..	..	92,000
2/29	.....	3,550,000	59	13,600	62	1	37	..	Many	106,000
3/2	.....	4,180,000	49	10,700	66	2	30	Transitionals 2	..	94,000
3/6	.....	3,610,000	49	11,100	61.5	14	22	1.5 Basophil 1	..	224,000
5/2*	.....	4,990,000	58	8,400	44	5	5	Large mononuclears, 3; transitionals, 1	..	354,000

* Coagulation time, 2½ minutes; bleeding time, 1½ minutes; no retraction of clot in twenty-four hours.

and tarry and tests for blood were positive. On rectal examination, abnormalities were not noted. On closer questioning, after the boy had been in the hospital several days, it was learned that he had occasional pain about the umbilicus and that at times he had been somewhat tender over this area. He described the area of pain as being enclosed in a circle which radiated about 2 inches from the navel. Because of the location and character of the pain and the enteral hemorrhage, together with the history of a previous attack of acute abdominal pain which simulated appendicitis, a diagnosis was made of Meckel's diverticulum with bleeding. The possibility of a thrombocytopenic blood dyscrasia was kept in mind. The Hess cuff test did not produce capillary hemorrhages. Gastroenteroroentgenologic examination, stasis meal and barium enema did not reveal abnormalities or lesions.

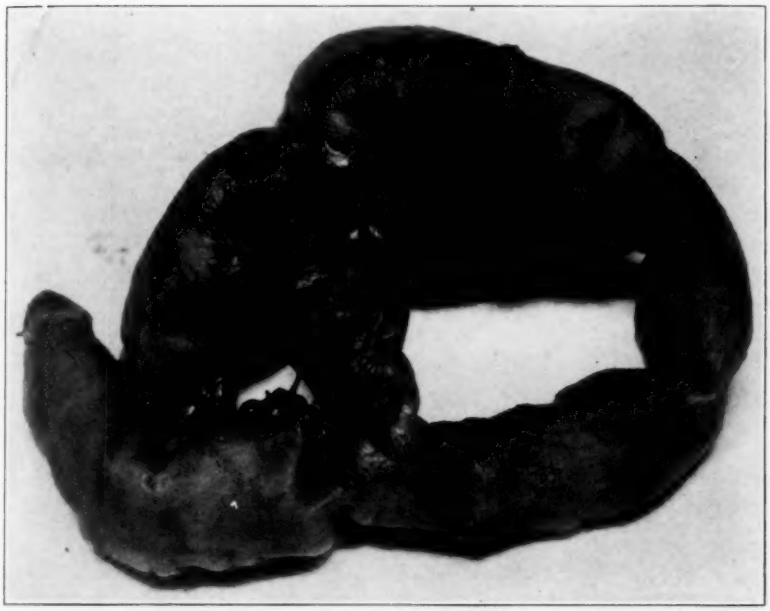

Fig. 1.—The section of ileum resected. The diverticulum may be seen arising from the lower loop and attached to the proximal (upper) loop.

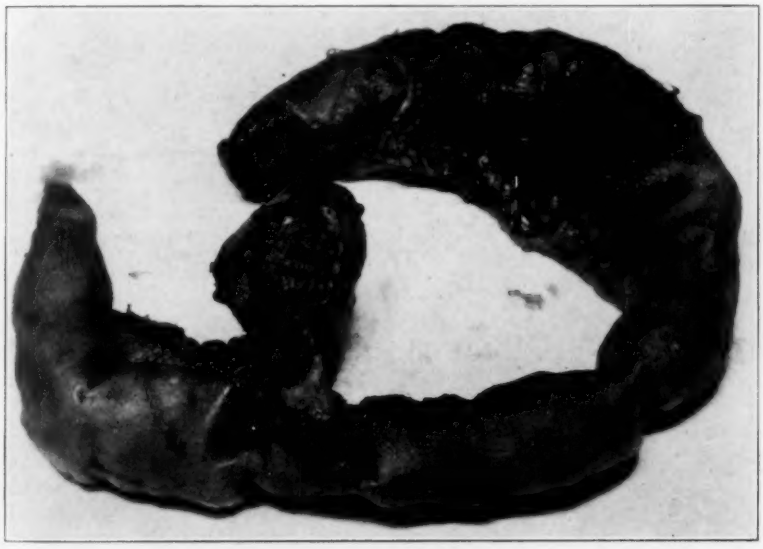

Fig. 2.—The diverticulum below with the tip detached from its bed in the loop above.

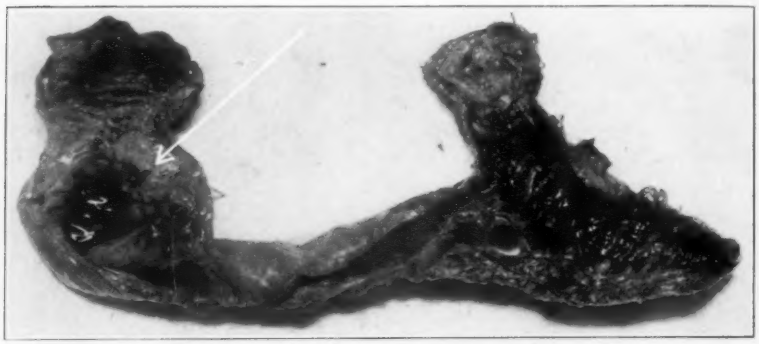

Fig. 3.—Loop laid open—diverticulum at right—tip lined with gastric mucosa. At left may be seen partial obstruction of ileum proximal to diverticulum. Arrow points to ulcer shown in figure 5.

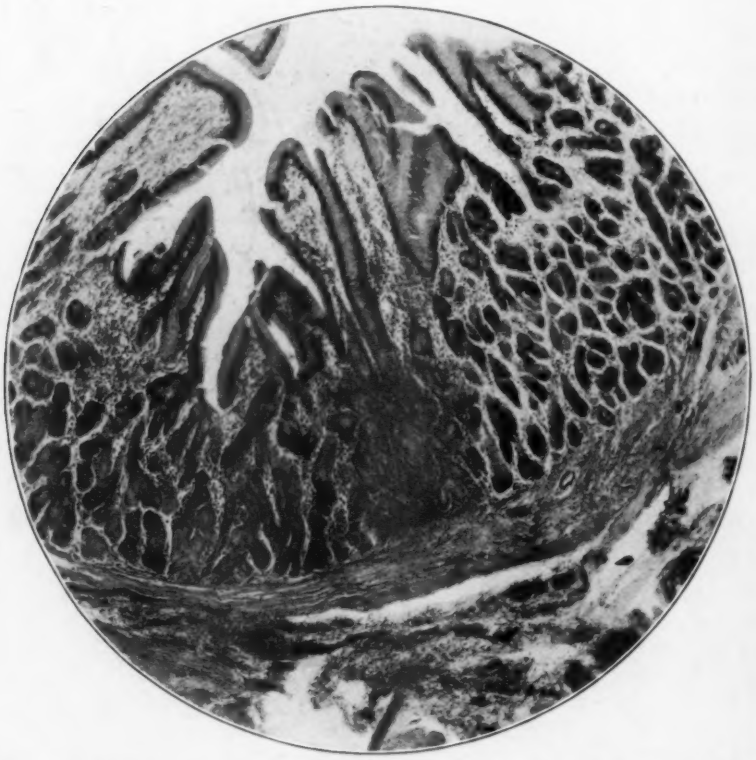

Fig. 4.—Section of gastric mucosa found in tip of diverticulum, showing parietal cells. Low power magnification.

The tarry stools continued, and on the fifth day 40 cc. of whole blood was injected into the buttocks, but the bleeding continued. On the sixth day, the boy complained of pain about the umbilicus. On the seventh day, the bleeding time was one minute and the coagulation time three and one-half minutes, with retractility of the clot in two hours. The van den Bergh test was negative. The Wassermann and microprecipitation tests were negative. The sedimentation rate of the red corpuscles (Westergren method) was increased and read: thirty minutes, 20 mm.; sixty minutes, 30 mm.; two hours, 80 mm.; twenty-four hours, 127 mm. Fragility of the red cells was: minimal resistance, 36 and maximal, 28;

Fig. 5.—Ulcer in ileum at point of attachment of tip of diverticulum, showing loss of mucosa, thickened muscularis and marked proliferation of connective tissue at base. Low power magnification.

control minimal, 40 and maximal, 30. On the eighth day, 300 cc. of citrated blood was transfused, and proctoscopic examination, under nitrous oxide anesthesia, was made. Lesions were not seen. The patient vomited yellow, liquid stomach contents which did not contain blood following the anesthetic. Operation was performed on the eleventh day after admission.

A straight right rectus incision was made. The appendix was found bound down at the middle by filmy adhesions and was long. A Meckel's diverticulum was found about 45 cm. proximal to the ileocecal valve. The diverticulum was about 4 cm. in length and had a broad base. It lay on the upper surface of the mesentery

of the small intestine. Its tip was adherent to the side of the ileum about 11.5 cm. above the point where the diverticulum was given off. When the diverticulum was separated from the wall of the bowel at this point, it was found that an ulcer had perforated through the wall of the ileum not communicating with the lumen of the diverticulum. At the point of perforation a thickening of the wall of the ileum, which was 2 cm. in diameter was found, and the wall of the bowel at the point of perforation was friable. It was decided for this reason to resect the ileum from above the point of perforation to a point below the diverticulum. This was done, about 28 cm. of ileum being resected, and the continuity of the intestine

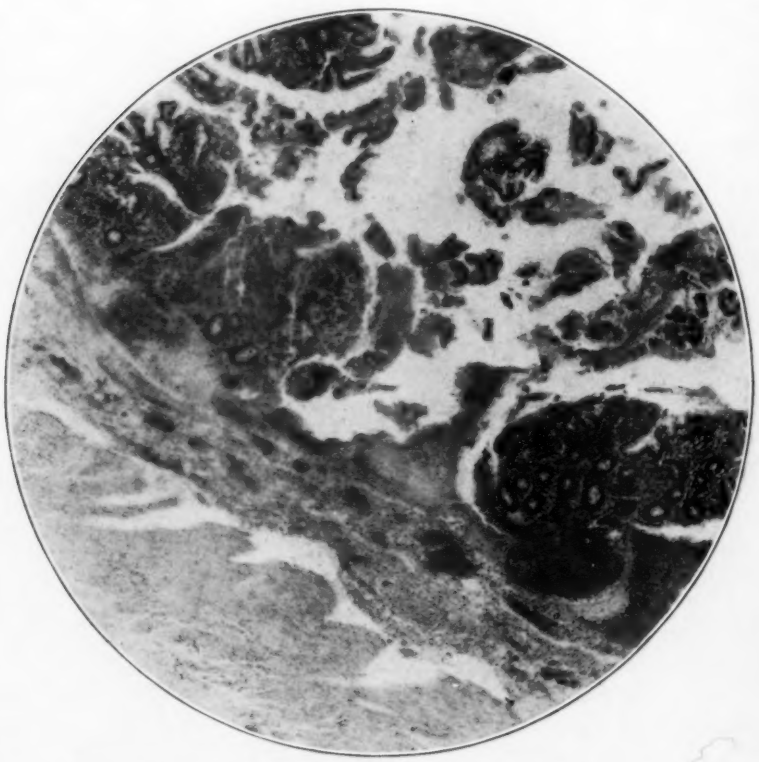

Fig. 6.—Ulcer in ileum distal to that in figure 5, showing erosion of mucosa and hemorrhage in submucosa. Low power magnification.

was restored by a lateral anastomosis. The appendix was also removed. The patient was moderately shocked by the operation, but made an uneventful recovery.

The specimen of resected ileum measured 28 cm. The attached diverticulum was 4 cm. in length and 2.5 cm. in diameter. The bulbous tip, laid open, measured 3 cm. across and was lined with gastric mucosa. The tip had been separated from a proximal loop of ileum, 11.5 cm. from the base of the diverticulum. At the site of the attachment of the tip, there was a fibrous thickening 2 cm. in diameter in the center of which was a perforating ulcer 4 mm. in diameter. The fibrous thickening extending half way around the ileum produced a partial obstruction

with a lumen of 4 mm. Above this the ileum was dilated. Two and five-tenths centimeters distal to the obstruction was an ulcer 25 by 10 mm. through the mucosa, and 5.5 mm. farther was a third ulcer 7 mm. in diameter. At the base of the diverticulum was an ulcer measuring 12 by 5 mm.

CONCLUSIONS

This case of Meckel's diverticulum presents several unusual features. The first hemorrhage was intraperitoneal and was probably associated with the attachment of the tip of the diverticulum to the loop of the

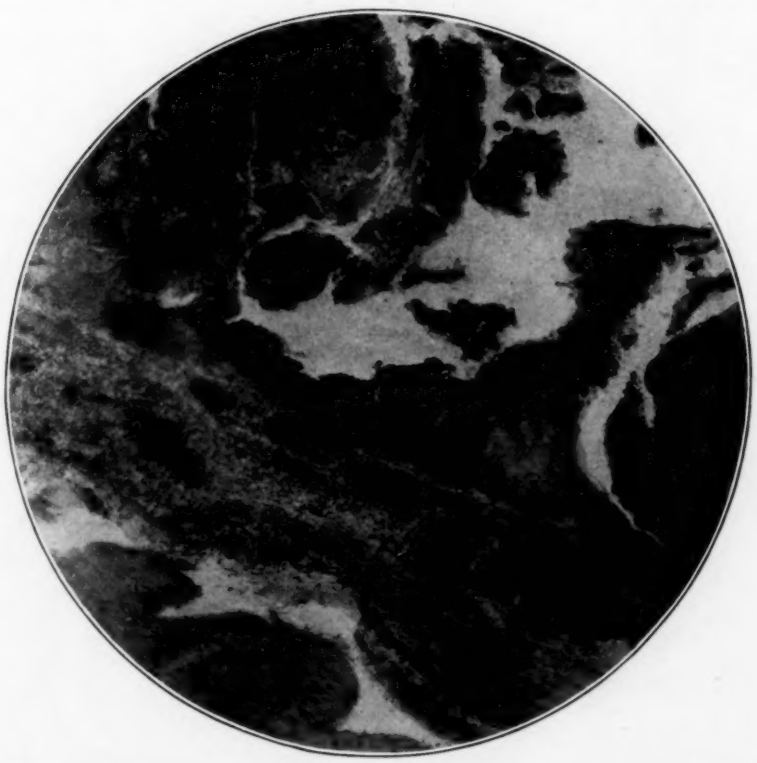

Fig. 7.—High power magnification of same area in figure 6, showing typical ulcer.

ileum. It is improbable that either the first or the second injury that the boy sustained had any relation to the intra-abdominal bleeding. This was probably caused by the inflammatory process resulting from the ulceration and perforation. The ulcer at the site of the perforation was the older. The second hemorrhage was entirely enteral and was associated with an infection of the upper respiratory tract. Thrombocytopenia was present throughout the course in the hospital, and the first clot did not show retractility. Except for epistaxis once, however,

there was bleeding only from the ulcers described. The ulcerations were multiple and occurred through the mucosa but were in the ileum and not within the diverticulum. Gastric mucosa was found in the tip of the diverticulum. In the differential diagnosis, thrombocytopenic purpura, tumor, varix, volvulus and intussusception were also considered.

167 Seventeenth Street.

DIPYLIDIUM CANINUM INFECTION IN AN INFANT SIX MONTHS OF AGE

REPORT OF A CASE *

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The occurrence of *Dipylidium caninum* as an intestinal parasite in an infant 6 months old is reported because its appearance in man is exceedingly rare, although it is commonly found in both the dog and cat.

REPORT OF A CASE

History.—W. V., a female infant, aged 6 months, was seen because the mother had noticed from time to time during the preceding five weeks, small white motile segments on the infant's diapers. The family history gave no evidence of parasitic infection, except that a boy, aged 14 years, boarding in the home, had from time to time been troubled with fleas acquired from a neighbor's dog. On one occasion, the mother had found a flea in the infant's carriage. No pets were kept in the home, and the environmental conditions were good. The past history was irrelevant. The infant had been breast fed successfully until five weeks prior to this visit, at which time a suitable pasteurized milk formula had been substituted without disturbance.

The segments had first been seen in the stools about the time the infant was weaned, or so shortly thereafter that infection must have occurred while the infant was entirely breast fed, three weeks being necessary for the development of an adult worm. The segments were at first thought to be pinworms, and treatment with enemas and catharsis was instituted. As a result of one large dose of castor oil, a chain of segments 2 or more inches in length was recovered, and this was recognized by the physician as segments of a tapeworm.

Examination.—Physical examination revealed a normal infant without any evidence of disturbance in nutrition, enlargement of the spleen or lymph nodes, and with normal blood findings. The stools contained an excess of mucous and occasionally, particularly after a cathartic, a segment would be found on the surface of a fecal mass or independently on the diaper.

After the diagnosis was confirmed, the problem presented itself as to whether treatment should be undertaken to rid the infant of the worm or whether this should be delayed until an age when a reasonable dose of some anthelmintic could be given with less probability of upsetting the digestion of the patient. As the amount of poison required to overcome an intestinal parasite is at least in a measure independent of the size of the host, it would seem unlikely that the adult dose of any anthelmintic proportioned down for an infant aged 6 months would be successful in destroying the worm. But the use of a large dose would seem to be accompanied by some risk to the health of the infant. It was therefore determined that unless it could be shown that the

* From the Departments of Pediatrics and Comparative Pathology, Harvard Medical School.

presence of the worm in the intestine over a long period of time was likely to do harm, delay in treatment was indicated. Such delay also offered the possibility that the parasite might be lost spontaneously, man being an unnatural and unusual host, and autoinfection from this variety being impossible.

Although the parasite is exceedingly common in dogs and present to a less extent in cats, pathologic conditions due to this parasite are apparently extremely rare in these animals. In the reported cases of infection in man, no symptoms referable to infection were noted. For these reasons, the infant was discharged without treatment but with instructions that periodic examinations should be made by the physician in charge so that treatment could be undertaken if evidences of harm from the infection should manifest themselves. It was felt that if segments still appear when the infant has reached the age of 18 months or more, treatment should be attempted regardless of symptoms.

LIFE HISTORY OF DIPYLIDIUM

Dipylidium caninum is one of the commonest intestinal parasites of pet dogs and cats and is occasionally found in man. It measures from 15 to 40 cm. in length and has a maximal breadth of from 2 to 3 mm. The scolex is small and rhomboidal, measuring about 0.55 mm. in diameter. The rostellum is claviform and is capable of retraction into a deep cephalic infundibulum. It is armed with three or four circlets of about sixty hooks shaped like a rose thorn. The hooks of the most anterior row are the larger, from 12 to 15 microns long. The hooks are easily lost, and specimens are often found without hooks or with only a few still in place. There are four fairly large, elliptical, unarmed suckers. The neck is short and thin. There are usually less than 200 proglottids in the entire chain. The mature and gravid segments are characteristically shaped like a vase or urn. Each proglottid has two sets of genital organs, and the genital pores lie symmetrically at the lateral margins. The vitellarium is some distance posterior to the ovary and is irregular and loosely lobulate. In *D. sexcoronatum*, the only other species of *D. caninum* reported from dogs of the United States, this structure is a relatively large and compact reniform structure. The onchospheres of *D. caninum* are round and measure from 35 to 40 microns in diameter. They are contained in nestlike cavities of the uterus and are seldom seen unless the proglottid becomes disintegrated or broken. Therefore, the diagnosis is best made from segments passed with feces from the patient.

The onchospheres of *D. caninum* are entirely different from those of *Taenia*. In the genus *Taenia*, there is a relatively thick, striated brown membrane (the embryophore) immediately surrounding the embryo, and the true egg-shell is often so thin and delicate a structure that it is easily dropped off and is seldom seen outside the proglottid. In *D. caninum*, the embryophore is thin and colorless and is surrounded by an albuminous coating outside of which is the egg-shell proper which is retained.

Life Cycle.[1]—Leuckart believed that an insect intermediate host was necessary for the completion of the life cycle of *D. caninum* but Melnikoff in 1869 was the first to demonstrate the larval form in the body of such a host, the dog louse, *Trichodectes canis.* In view of the fact that *T. canis* is not a frequent parasite of dogs and cats, it soon became apparent that this louse could not be the only intermediate host for this parasite. In 1880, Grassi found that it could also develop in the dog flea, *Ctenocephalus felis,* and in the human flea, *Pulex irritans.*

As in the case of many tapeworms, the gravid segments of *D. caninum* are carried along with the host's feces to the outer world, where they disintegrate and the enclosed onchospheres become scattered. Some of the onchospheres which eventually get into the fur of the dog or cat are ingested by the louse, *Trichodectes,* as it feeds on the skin of the dog, and in its body cavity they develop into the infective stage. In the case of the fleas, however, the eggs are ingested, while the fleas are larvae feeding on débris. The adult fleas are adapted to feed on blood and are unable to ingest a tapeworm egg. The onchospheres remain more or less unchanged in the adipose tissue and muscles of the flea larva during its various developmental stages until the adult emerges, at which time they develop into pear-shaped bodies within which are the invaginated head and suckers of the future tapeworm. This larva is known as a cysticercoid and is the only infective stage for the definitive host.

When the dog or cat takes up an infected flea by biting itself or by licking its fur, the cysticercoid becomes free in the intestine, and after attaching itself to the wall of the intestine quickly grows into the adult worm. Sexual maturity is reached in about twenty days. As many as fifty cysticercoids have been found in the body cavity of a single flea, therefore a rather heavy infection may result from the ingestion of a single infected flea.

Infection in man is entirely accidental and is evidently transmitted through the practice of allowing dogs to lick the face, at which time the flea is ingested, or through contamination of food. Infection in man, as well as in other definitive hosts, can be acquired only by the swallowing of the infected adult flea or louse. There are now about eighty records of its occurrence in man. Most of these cases are European. It is exceedingly rare in the United States, apparently having been recorded, as far as we are aware, but three times (Hall,[2] 1917). It is of particular interest to note that the majority of the infections in man have occurred in young children, many of whom were of the nursing age.

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1. Joyeux, C.: The Life Cycle of Some Cestodes, Bull. biol. de la France et de la Belgique, 1920.

2. Hall, M. C.: Parasites of the Dog in Michigan, J. Am. Vet. M. A. **4**:386, 1917.

Progress in Pediatrics

THE BACTERIOLOGY AND SEROTHERAPY OF MEASLES

A HISTORICAL AND CRITICAL REVIEW OF LITERATURE ON EXPERIMENTAL ASPECTS OF MEASLES *

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LOS ANGELES

The status of measles among the infectious diseases of infancy and childhood appears to have changed within the last twenty-five years, primarily owing to the increasing percentage of mortality as compared with that of other acute diseases, notably diphtheria and scarlet fever. The 10,000 annual deaths from measles and its complications, as recorded in the registered area of the United States, allow no optimism either on the part of the laity or on the part of the medical profession. Debré and Joannon [1] reported that during the first decade of the present century, measles occupied the foremost place in the causes of child mortality, claiming, as it actually did, a formidable aggregate of about 1,000,000 juvenile victims in the principal countries of Europe.

To combat the ravages of this disease, many able minds of Europe and America have long been mobilized to work out a means of practical strategy. It now seems certain that various mechanical methods of disinfection and quarantine, important as they are, can never control the disease clinically or epidemiologically. The trend of modern researches on measles seems to assume the line of biologic methods, which include: (1) bacteriology, (2) experimental inoculation in man and animals, and (3) prophylactic and therapeutic application of these results of study. In this paper I aim at a historical and critical review of these aspects of researches, which may aid in evaluating the relative merits of the various discoveries as they are applied in the conquest of the disease.[2]

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* Read at the monthly staff meeting of the Children's Hospital, Los Angeles, Jan. 12, 1928.

1. Debré, R., and Joannon, P.: La Rougeole: Épidémiologie, Immunologie, Prophylaxie, Paris, Masson & Cie, 1926, p. 18.

2. In the preparation of the present paper, the following general reviews have been of the greatest value: Zeiss, H.: Die Experimentelle Masernübertragung, Ergebn. d. inn. Med. u. Kinderh. **2**:492, 1921. Schmidt, H.: Med. Klin. **16**:933, 1920. Thomas, L.: Measles, in Ziemssen: Cyclopedia of Practical Medicine, 1878, vol. 2, p. 31. Gröer, F. von, and Redlich, F.: Der gegenwartige Stand der biologischen Masernprophylaxe, Ergebn. d. inn. Med. u. Kinderh. **30**:506, 1926.

BACTERIOLOGY OF MEASLES

In spite of the warning by Zinsser [3] to the effect that "it would be a thankless task to review the literature of all the many attempts to isolate micro-organisms from this disease, none of which has resulted in throwing any light on the etiology," I shall devote a little space to the bacteriology of measles, for it will furnish a certain fundamental point of view in proper evaluation of immunologic and therapeutic facts. At the outset it must be frankly admitted that the causative agent in measles has not yet been established with final certainty, although the normal habitat of the contagium during the course of the disease has been known for fifty years or so. As early as 1878, Thomas [4] remarked:

> From the results of inoculations, the propriety has been inferred of regarding it (the causative organism) as present in the blood, especially that of the measles spots, upon the skin, in the contents of the miliary vesicles which develop upon these spots, in the tears, and the secretion of the nasal mucous membrane, perhaps also in the saliva and in the sputa.

The early investigators seem to have focused their attention on one or other forms of *Protozoa* as a possible cause of measles. Salisbury [5]

Marie, P. L.: Recherches recéntes sur la rougeole, Presse méd. **30**:456 (May) 1922; ibid. **30**:711 (Aug.) 1922. Robinson, E. S.: Recent Progress in the Prevention and Treatment of Scarlatina, Measles and Diphtheria, Fiske Fund Prize Essay, no. 62, Providence, 1926. Combay, J.: Traitement prevéntif de la rougeole, Arch. d. méd. d. enf. **25**:614, 1922. Debré, R., and Joannon, P.: La rougeole: épidémiologie, immunologie, prophylaxie, Paris, Masson & Cie, 1926. Pollitzer, R.: Revue des recherches sur l'étilogie et la pathogenie de la rougeole, Presse méd. **33**:1269 (Sept. 23) 1925. Sellards, A. W.: A Review of the Investigations Concerning the Etiology of Measles, Medicine **3**:99 (May) 1924. Ashe, B. I.: Specific Aspects of Measles, Arch. Pediat. **41**:375 (June) 1924. O'Hara, D.: Recent Progress in Prevention and Treatment of Scarlatina, Measles and Diphtheria, Boston M. & S. J. **195**:561 (Sept. 16) 1926. McCartney, J. E.: A Review of Recent Work on Measles, Lanet **1**:93 (Jan. 8) 1927. The article by Hektoen: Experimental Measles, J. Infect. Dis. **2**:238, 1905, gives the best review of early experiments on human inoculation, from which the data are freely drawn. The monograph by Pirquet: Das Bild der Masern auf ausseren Haut, Ztschr. f. Kinderh. **6**:1, 1913, is most instructive in the hypothesis of measles eruption, and gives a rather full bibliography on measles since 1890. The monograph by Debré and Joannon also contains an extensive bibliography, although it is rather incomplete in citations. The earlier references are found in the article by Thomas in Ziemssen: Handbuch der speciallen Pathologie und Therapie, 1877, vol. 2, p. 32. A comprehensive list of more important references is also furnished by Robinson in his Fiske prize essay.

3. Zinsser, H.: A Textbook of Bacteriology, ed. 6, 1927, p. 780.

4. Thomas, L. (footnote 2, third reference).

5. The original sources for this and all subsequent references on the bacteriologic reports of individual authors are given in chronological order in table 1, to which the reader is referred for verification. Footnote references are given only for the citations not given in this table.

was the first to report on the discovery of a measles organism. In 1862, he published an account of a certain fungus spore found in decaying straw, with which he inoculated several persons and obtained an exanthem bearing a close resemblance to measles, probably the so-called "camp measles;" later, however, Pepper [6] inoculated twenty-two persons with the same fungus without causing any effect, even though all of his subjects had not had the disease before. Behla stated that the disease was caused by *Sporozoa* found in the blood and nasal mucosa of patients. Eklund discovered an organism in the sputums, urine and blood of patients with measles, which he named *"Torula morbillorum."* Doehle found ameba-like bodies in the red corpuscles, which he associated with the cause, and Rosenberger saw similar bodies. Hlava claimed to have seen Leishmann-like bodies in the blood cells, while Costa published an account of blastomycetes as being responsible for the disease.

Most of the foregoing investigators who associated measles with various forms of higher bacteria were apparently looking at some form of inclusion bodies in the erythrocytes, as well as at those found free in the plasma, representing the products of cell degeneration due to the action of bacterial toxins. At any rate, these older observations have not since been confirmed. Field,[7] after studying some of the supposedly protozoan organisms which had been described, concluded that "they were not protozoa but that they were probably degenerating and cytolysed epithelial cells and leukocytes, which within certain limits are specific for measles and scarlet fever." Likewise, Ewing [8] remarked, "Although in the epithelial cells are found many structures which bear some resemblance to protozoa, yet the general characters of the disease, and especially the widespread occurrence of acute degeneration and necrosis of epithelial cells, all suggest that measles is referable to infection by a bacterium which produces an active toxin having especial affinity for superficial cells." Heubner [9] gave the gist of bacteriologic problem when he said, "Only a specific poison developing anew in man is capable of producing the disease." The modern experimental investigations on measles are directed toward the search for a bacterium specific for measles.

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6. Pepper, cited by Thomas, in Ziemssen: Handbuch für specifische Pathologie, 1877, vol. 11, p. 29.

7. Field, C. W.: On the Presence of Certain Bodies in the Skin and Blister from Scarlet Fever and Measles, J. Exper. Med. **7**:343 (July) 1905.

8. Ewing, J.: Epithelial Cell Changes in Measles, J. Infect. Dis. **6**:1 (Jan. 1) 1909.

9. Heubner, O.: Measles, in Modern Clinical Medicine, Volume on Infectious Diseases, 1911, p. 309.

TABLE 1.—*Chronological List of Bacteriologic Reports on Measles*

Author and Source	Micro-Organism	Habitat	Culture and Inoculation
Salisbury, J. H.: Am. J. M. Sc. **44**: 17 and 87, 1862	Fungus spore	Decaying straw	Measles produced by human inoculation
Hallier, E.: Centralbl. f. d. med. Wissensch. **6**: 161, 1868	Cocci with tail-like end, movable and colorless	Blood and sputums	Failed to culture
Coze and Feitz: Recherches cliniques et expérimentales sur les maladies infectieuses. Paris, 1872	Bacteria of great activity and extreme delicacy	Blood, nasal mucus measles spots	Blood inoculation in rabbits, followed by fever for 2 to 3 days
Klebs, E.: Verhandl. d. phys.-med. Gesellsch. in Würzburg, 1874	Specific micrococcus of measles	Trachea and heart's blood	
Braidwood, P. M., and Vacher, F.: Brit. Med. J. **1**: 77, 1882	Sparkling, staff-shaped fusiform or ovate bodies	Breath, skin and lungs	
Keating, J. M.: Phil. Med. Times **12**: 765, 1882	Micrococci	Blood in malignant cases	
Babesiu: Pest. méd.-chir. Pressé **17**: 60, 1881	Spherobacteria		
Eklund, A. F.: Ann. de dermat. et syph. **3**: 405, 1882	"Torula morbillorum" 1.5 micron in diameter	Blood, eruptions urine	
Le Bel, J. A.: Compt. rend. Acad. d. Sc. **96**: 68, 1883	Spore-forming vibrio	Urine and skin eruptions	Pathogenic for animals
Tobeitz, A.: Arch. f. Kinderh. **8**: 321, 1886-1887	Staphylococcus, streptococcus	Necrotic lung tissue and bronchial secretions	
Cornil, A. V., and Babes, V.: Les bactéries et leur rôle dans l'anatomie et histologie, Paris, 1886	Streptococcus (in one case, very short bacillus)	Blood, lung tissue, lymphatics	Produces fever, conjunctivitis and erythema in guinea-pigs
Canon, P., and Pielicke, W.: Berl. klin Wchnschr. **29**: 377, 1892	Short, gram-negative bacillus	Blood, sputum, nasal and conjunctival secretions	No growth on bouillon and blood-agar mediums
Doble, P.: Centralbl. f. allg. Pathol. u. path. Anat. **3**: 150, 1892	Ameba-like bodies, spindle-shaped	Red blood corpuscles	
Czaikowski, J.: Centralbl. f. Bakteriol. **18**: 517, 1895	Diplobacterium, very small, with rounded ends; gram-negative	Blood and nasal secretions	Grows well on ascites, glycerin agar and blood serum; not pathogenic for puppies, but mice die of septicemia
Behla, R.: Centralbl. f. Bakteriol. **20**: 561, 1896	Sporozoa	Blood and nasal mucus	
Barbier, H.: Bull. et mém. Soc. méd. d. hôp. de Paris **14**: 141, 1897	Diphtheria bacillus	Conjunctiva	Obtained in pure culture
Ostrovsky, E.: Congr. internat. de. méd. **2**: 174, 1897	Mobile diplococcus, with halo from 0.2 to 0.7 microns in diameter; gram-negative	Blood in preeruptive stage; pure culture in saliva	Grows in alkaline hay infusion, with 1% hemoglobin; pathogenic for mice, guinea-pigs and rabbits
Arzamasskoff, G. E.: Bolnitch. Gaz. Botkina. St. Petersburg **40**: 1949, 1898	Short rod, drumstick shape, with dark brown pigments	Blood, conjunctival and nasal secretion	Grows on blood and glycerin agar, forming a small colony
Lesage, M.: Compt. rend. Soc. de biol. **52**: 203, 1900	Gram-negative micrococci	Blood, nasal and pharyngeal secretions	Puppies die in from 2 to 20 days of hemorrhagic septicemia
Giarré, C., and Picchi, L.: Clin. mod. **6**: 178, 1900	B. influenzae, resembling diplococcus aureolatus; gram-negative	Conjunctiva and nasopharyngeal	Culture only on blood agar, reaching maximum on third day; reinjection gave negative result
Pinna, G., and Marini, G.: Policlinico **7**: 347, 1900	Hemorrhagic staphylococcus	Measles scales	No definite proof
Van Niessen, M. A.: Arch. f. Dermat. u. Syph. **60**: 429, 1902	"Micrococcus roseus"	Blood	

TABLE 1.—*Chronological List of Bacteriologic Reports on Measles—Continued*

Author and Source	Micro-Organism	Habitat	Culture and Inoculation
Armand-Delille, P.: Arch. d. méd. d. enf. **5**: 202, 1902	Pseudodiphtheria bacillus		
Fenoglio, I.: Jahrb. f. Kinderh. **55**: 109, 1902	Staphylococcus		
Pacchioni, D.: Atti. d. accad. med.-fis. florent. **33**: 39, 1902	Hemophilic bacillus		
Mayer, A.: München. med. Wchnschr. **31**: 733, 1904	Very small, rod-shaped bacilli, in pairs, and immobile	Contents of papule, conjunctival and nasal secretions	Grows on blood agar and ascites gelatin; gram-negative; nonpathogenic for animals
Zlatogoroff, S. J.: Russk. Vrach. **3**: 981, 1904	Gram-positive bacilli with round ends	Blood	Grows in sediment of fluid medium containing human blood; animal inoculation negative
Schottelius, von E.: München. med. Wchnschr. **51**: 378, 1904	Staphylococcus aureus, streptococcus and diphtheria bacteria	Conjunctival secretion, lungs and spleen on autopsy	
Menschikow, W. K.: Russk. Wratsch. no. 26; Zentralbl. f. Bakteriol. **37**: 496, 1905	Diplococcus and influenza bacillus; diplostreptococcus brevis	Sputum, secretions of pharynx, conjunctiva and ear	Grows on blood agar; gram-negative
Borini, A.: Riforma med. no. 25; Zentralbl. f. Bacteriol. **40**: 194, 1905	Long, slender, gram-positive bacillus	Blood, conjunctival and bronchial secretions	Pathogenic for dogs and puppies; resembles that of Czaikowski and Zlatogoroff
Gundobin, N. P.: Vrach Gaz. p. 1029, vol. 12; cited by Kolle u. Wassermann, (1913) vol. 8, p. 464	Short, feebly motile bacillus	Blood and nasopharynx of 60 of 64 patients	Agglutinated by 1:200 measles serum; animal serum immunized by this bacillus has favorable effect on course
Rosenberger, R. C.: Amer. Med. **12**: 139, 1906	Ameba-like body	Red blood cells	
Cannata, S.: Clinica med. ital., no. 6; Zentralbl. f. Bakteriol. **42**: 203, 1909	Micrococcus tetragenus; Staphylococcus albus	.....	In puppies, symbiosis of these two organisms has a peculiar virulence
Sittler, P.: München. med. Wchnschr. **61**: 2705, 1909	White cocci and Staphylococcus pyogenes	Secretions from mouth, nose and eye, but never in blood	Anaphylaxis with filtered bouillon culture; white coccus agglutinated by 1:200 immune serum
Lorey, A.: Ztschr. f. Hyg. **63**: 135, 1909	Streptococcus erysipelatis and pneumococcus	Tonsils, middle ear secretions and blood	
Ciacco, C.: Virchows Arch. f. path. Anat. **199**: 278, 1910	Gram-positive rod (diphtheroid)	Eye, nose, larynx and tonsils; inner organs	
Hlava, J.: Franz-Josephs-Akad., 1910; cited by Zeiss, H.: Ergebnis. d. inn. Med. u. Kinderh. **20**: 492, 1921	Leischmann-like bodies	Red blood cells	
Strauch, F. W.: Ztschr. f. Hyg. **65**: 183, 1910	Streptococcus pneumococcus	Blood	
Iwanow: Med. Obozr., no. 64; cited by Kolle u. Wassermann, 1913, vol. 8, p. 464	Short bacillus with round edges	.....	Serum of measles patients agglutinates at 1:100; pathogenic for puppies and white mice
Costa, S.: Compt. rend. Soc. de biol. **74**: 62, 1913	Blastomycetes	Blood	
Tunnicliff, R.: J. A. M. A. **68**: 1928 (April 7) 1917	Very small, green producing diplococcus; gram-positive	Blood and nasal secretion	Grows only in anaerobic mediums containing blood; specific skin test and agglutinin and opsonin identified
Sellards, A. W., and Strum, E.: Bull. Johns Hopkins Hosp. **30**: 331, 1919	B. influenzae		

TABLE 1.—*Chronological List of Bacteriologic Reports on Measles—Continued*

Author and Source	Micro-Organism	Habitat	Culture and Inoculation
Sellards, A. W., and Bigelow, G. H.: J. Med. Research **42**: 241, 1921	Diphtheroid; gram-positive pleomorphic bacilli	Blood and conjunctiva	Feeble growth in original; luxuriant in subcultures; inoculation into monkeys produces suggestive rash
Degkwitz, R.: Monatschr. f. Kinderh. **22**: 186, 1921; J. Infect. Dis. **41**: 304, 1927	Filtrable virus	Blood	Grown best in fluid mediums containing human serum; the virus can be kept alive for several weeks, if diluted 1:7-1:10 with buffered salt solution at 0 C.
Salimbien, A. T., and Kermorgant, Y.: Compt. rend. Acad. d. sc. **177**: 717, 1923	Spirochete	Blood and urine	Isolated in proper medium
Caronia, G.: Pediatria **31**: 801, 1923; **32**: 888, 1923	Small diplococcus	Blood, nasopharyngeal secretions, cerebrospinal fluid, urine, scales, bone-marrow, internal organs	Grows on anaerobic, catalyzing mediums of Di Cristina or Tarrozzi-Noguchi type; specific agglutinin, opsonin and amboceptor are found in immune serum; specific skin test demonstrated
Thomson, D.: J. Trop. Med. **26**: 227, 1923; Ann. Pickett-Thomson Res. Lab., **1**: 77, 1924; **2**: 1, 1926	Diplococcus; gram-negative very minute (0.3 micron)	Swabs from throats	Strict anaerobe, growing only on mediums containing plasma, whole blood, hydrocele fluid, or testicular extract; (significance doubted later)
Kusama, S.: Tokyo Iji-Shinshi, no. 2397, 1924	Gram-positive bacillus, with deep-staining round bodies at ends	Kidney, removed from patient at autopsy	Not filtrable, growing best in ascites fluid medium; pink color produced; agglutination titer 1:10
Hibbard, R. J., and Duval, C. W.: Proc. Soc. Exper. Biol. & Med. **23**: 853, 1926; **24**: 519, 1927	Gram-positive coccus, corresponding to that described by Tunnicliff	Blood and nasopharyngeal secretions	Grows on semisolid plasma medium or hydrocele fluid, later on ordinary blood agar slants
Flesch, M.: München. med. Wchnschr. **73**: 1480, 1926	Small rods	Blood	Direct microscopic examination of smear on 7th day
Ferry, N. S., and Fisher, L. W.: J. A. M. A. **86**: 932, (March 27) 1926	Streptococcus morbilli; small gram-positive green producing, appearing in pairs and chains	Blood	Grows luxuriantly in aerobic conditions, producing soluble toxin, neutralized by blood of convalescents; specific skin test
Long, E. H., and Cornwell, A. M.: J. Infect. Dis. **40**: 408, 1927	Negative results in 47 blood cultures taken from 26 patients		
Cary, W. E., and Day, L. A.: J. A. M. A. **89**: 1206 (Oct. 8) 1927	Small green-producing, gram-positive, short chained streptococcus	Blood, throat and conjunctival secretions	Grows aerobically on sheep blood agar; rabbits injected with 10 cc. of bouillon culture gave febrile response

In order to make the review complete, it is necessary to mention briefly the various organisms usually thought to be specific for diseases other than measles which many workers believe bear etiologic relations to measles. The diphtheroid bacillus was first reported by Barbier, and later by Ciacco and Sellards and Bigelow. Mallory and Medlar,[10] more-

10. Mallory, F. B., and Medlar, E. M.: Skin Lesions in Measles, J. M. Reseach **41**:327 (March) 1920.

over, found this bacillus rather constantly in many slides and sections as well as in smears of mucous secretions removed at autopsy from patients with measles. *Bacillus influenzae* was thought to be vitally connected with measles by a large number of observers, such as Paltauf, Albrecht, Gehle, Süsswein, Liebscher, Giarre and Picchi, Sellards and Strum and others. Other observers believe that other organisms are related to this disease. Pneumococcus was advanced by Strauch and Lorey; pleomorphic spirochetes by Salimbien and Kermorgant; globuriform bacillus by Arloing and Dufourt; pleomorphic bacilli by Sellards and Bigelow; gram-positive bacilli with round ends by Kusama, Borini, Zlatogoroff; *Micrococcus tetragenus* by Cannata; bacteria of great activity by Coze and Felts; spore-forming vibrio by Le Bel; staphylococcus and streptococcus by Cornil and Babes, Tobeitz, Fenoglio and Schottelius; short gram-negative bacilli by Canon and Pielicke, Gundobin, Iwanow and Flesch; diplobacterium by Czaikowski; short rod, drum-stick like gram-negative bacilli with dark yellowish pigments by Arzamasskoff; hemolytic staphylococcus by Pinna and Marini and *Streptococcus erysipelatis* by Lorey.

The foregoing miscellaneous bacteria, no matter how extensive the reports on them may have been, now appear to be totally missing the mark. Some observers were looking at the bacteria of complications and perhaps of contaminations, while others those of mere coincidence or of symbiosis. It is possible that some were looking at the true causative bacterium, but failed to make a fuller morphologic and immunologic identification. The more recent studies, with a more adequate scientific control, seem to be unanimous that the bacterium concerned in the etiology of measles is a form of micrococcus which can be isolated with comparative ease under proper cultural conditions.

The first micrococcus, in the form of a diplococcus, was seen by Ostrovsky in 1897, who found it in great abundance in the sputum and blood of patients suffering from measles, although as early as 1869, Hallier had described it and it had been emphasized by many subsequent bacteriologists. The micrococcus is described by Hallier as "cocci with tail-like ends," by Bebesiu as "spherobacteria," by Klebs as "specific micrococci of measles," while Braidwood and Vacher called it merely "spheroid bodies." Other names given to this (probably the same) micrococcus are "gram-negative micrococcus" (Lesage), *"Micrococcus roseus"* (van Niessen), *"Diplostreptococcus brevis"* (Menschikow), "green-producing diplococcus" (Tunnicliff, Hibbard and Duval, Cary and Day), "very minute but true diplococcus" (Thompson, "small anaerobic diplococcus" (Caronia) and *"Streptococcus morbilli"* (Ferry and Fisher).

Whether or not all these investigators who saw micrococci in one form or another in close association with typical cases of measles are

speaking of one and the same organism remains to be proved. In all probabilities, they are all talking of the same micro-organism, although there are certain discrepancies emphasized by each due primarily to variations in the cultural methods employed, as Hoyne and Gasul [11] would infer. At any rate, the various forms of *Micrococcus* are considered by many accurate observers to be the most probable organism specifically related to the etiology of measles.

The first extensive work on micrococcus of measles was done, as already referred to, by Ostrovsky in 1897, who, basing his observations on sixty-four cases of measles, isolated and described a mobile organism in the form of a diplococcus surrounded by a halo and measuring from 0.2 to 0.7 microns in diameter, which can be cultivated in a slightly alkaline hay infusion containing 1 per cent hemoglobin, and killed by cooling to 40 C. It is gram-negative. It is found in the blood from the first day of the exanthem up to the seventh or even the fourteenth day, when there is no defervescence. It can be found almost in pure state in the saliva and in the nasal and conjunctival secretions during the first hours of the exanthem, or in the preeruptive stage. When inoculated into white mice or guinea-pigs, this organism causes death of animals in from three to eight days. Intravenous injection into the rabbit causes an acute but not a fatal infection lasting fifteen days, with elevation of temperature, injection of conjunctival mucosa, humidity of the nares and loss of weight. The filtrate of a twenty day culture of this organism also causes the same signs of infection in rabbits.

The work of Ostrovsky, interesting from a historical point of view, has not been followed up either by the original investigator himself or by others. Hence one can compare the organism of his description only with those mentioned in the more extensive work of later writers, of whom Tunnicliff and Caronia stand foremost.

In the first publication of her epoch-making paper in 1917, Tunnicliff [12] of Chicago described a green-producing diplococcus isolated from

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11. Hoyne, A. L., and Gasul, B. M.: Measles Prophylaxis, J. A. M. A. **87:** 1185 (Oct. 9) 1926.

12. The work of Tunnicliff and her associates at the John McCormick Institute for Infectious Diseases, Chicago, on the bacteriology of measles is published in the following articles: Tunnicliff, R.: Cultivation of a Micrococcus from Blood in Preeruptive and Eruptive Stages of Measles, J. A. M. A. **68:**1028 (April 7) 1917; On the Bacteriology and Immune Reactions of Measles and Rubella, J. Infect. Dis. **22:**402, 1918; Observations on Throat Smears in Measles, Rubella and Scarlet Fever, J. A. M. A. **71:**104 (July 13) 1918. Tunnicliff, R., and Brown, M. W.: Immune Reactions with Diplococci Isolated from Measles and Rubella, J. Infect. Dis. **23:**572, 1918. Tunnicliff, R.: Agglutination in Measles, ibid. **24:**76, 1919; On the Bacteria in the Sputum in Measles, ibid. **24:**181, 1919. Tunnicliff, R., and Moody, W. B.: Experimental Measles with a Diplococcus,

(Footnote continued on following page)

the blood of persons with measles in the preruptive and eruptive stages. It is a small, round, sometimes flattened, diplococcus or is in short chains, sometimes in clumps of cocci of varying sizes. It is gram-positive and stains well with ordinary stains. It passes through Berkefeld filter "N," and resists drying for twenty-four hours, but does not live after forty-eight hours. It is killed by heating at 57 C. for forty-five minutes and resists a temperature of —2 C. at least fourteen days and 50 per cent glycerin two months at least. This organism was subsequently found in the nasopharyngeal and conjunctival secretions and sputum of patients with measles. It was further found that the blood of patients convalescing from measles contained specific agglutinins, opsonins and complement-fixing antibodies for this diplococcus. Still later, Tunnicliff and Taylor, using the filtrates of cultures grown from six to seven days in 1 per cent sheep blood, 0.2 per cent dextrose broth, obtained a definite skin reaction in a dilution of 1:10 in susceptible persons. The reaction consisted of a circumscribed area of erythema about 1 cm. in diameter, appearing in from eight to twenty-one hours after the intradermal injection of 0.1 cc. of the foregoing dilution. From this experiment, they concluded that this green-producing diplococcus produces an extracellular toxin which gives a definite skin reaction in persons with a negative history of measles, but in 96 per cent of those with a positive history a reaction is not obtained. The inoculation of this organism by Tunnicliff and Moody into rabbits, guinea-pigs and monkeys gives rise to the same symptoms as when they are inoculated with nasopharyngeal washings. Furthermore, the blood of animals so inoculated contains this diplococcus, and this blood is capable of producing Koplik spots and exanthems when injected into other animals. Further studies by Tunnicliff show that this organism is immunologically distinct from nearly all similar cocci isolated during convalescence. Her studies answered the questions raised by Park and Williams by showing that when the organism is grown in normal and immune horse serum, dextrose broth loses its specificity, as determined by the opsonic method, but regains it after transfer onto blood agar at 36 C. for a few generations; and that growth of the organism at from 40 to 41 C. completely removes its specificity. The most recent work of Tunnicliff concerns the production of measles antiserum on a commercial scale, so as to enable its universal application for therapeutic purposes.

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ibid. **31**:382, 1922. Tunnicliff, R.: Further Studies on a Diplococcus in Measles: A Measles Skin Reaction, ibid. **37**:193, 1925. Tunnicliff, R., and Taylor, R. E.: Skin Tests in Measles, J. A. M. A. **87**:846 (Sept. 11) 1926. Tunnicliff, R.: Further Observations on the Specificity of the Green-Producing Diplococcus in Measles, J. Infect. Dis. **41**:267, 1927.

In 1923, Caronia [13] and his associates in the pediatric clinic at Rome published a series of articles relating to the discovery of the causative agent in measles. They succeeded in cultivating a micro-organism from the blood, bone-marrow, nasopharyngeal exudate, cerebrospinal fluid, urine and desquamated skin of patients with measles. It can be cultivated in infinite series in the special mediums of Di Cristina and Tarrozzi-Noguchi and other anaerobic conditions, but there is rather a scanty development of visible forms. It is round, very small, from 0.3 to 0.4 micron in diameter, often in pairs like a diplococcus and surrounded by a slight, clear halo. It stains well with the usual aniline stains, especially Loeffler's blue; it is gram-negative. In all probability it multiplies by fission. It passes through an ultramicroscopic stage as it can be filtered through the densest filters. It has been found microscopically in the liver and kidneys of animals that have been infected experimentally. Ritossa [14] found the organism in the spleen, the liver and the kidneys of the still-born baby of a woman sick with measles. He carried out a series of serologic studies and found an agglutinin, an opsonin and an amboceptor for this organism in the serum of patients with measles. The immune reaction appears in the first days of the disease and increases in strength and is still present after recovery. De Villa,[15] giving intramuscular injections of 0.1 cc. of killed cultures or of filtrate from cultures to healthy children or to children sick or convalescing from measles, in 63 per cent of the susceptible persons, observed a special reaction characterized by swelling and redness, while in 75 per cent of those sick or convalescing from measles and in 83 per cent of those who had been vaccinated with Caronia's antimorbillous

13. Caronia, G.: Ricerche sulla etiologia de morbillo, Pediatria **31**:801 (Aug. 1) 1923; Deutsche. med. Wchnschr. **50**:232 (Feb. 22) 1924; Presse méd. **31**:877 (Oct. 20) 1923; abstr., J. A. M. A. **81**:1152 (Sept. 29) 1923. Other important work on Caronia's organism carried on and published by his associates are: Sindoni, M. B.: Caratteri morfologici e culturali del germe del morbillo, Pediatria **32**:888 (Aug. 1) 1924; abstr., J. A. M. A. **83**:878 (Sept. 13) 1924. Ritossa, P.: Sulla presenza del germe del morbillo negli elementi eruttivi, nelle squame nelle urine, ibid. **32**:346 (March 15) 1924; abstr., J. A. M. A. **82**:1305 (April 19) 1924. Catteruccia, C.: Sulla presenza del germe del morbillo nel liquido cefalo rachidiano, ibid. **32**:1101 (Sept. 15) 1924; abstr., J. A. M. A. **83**:1462 (Nov. 1) 1924. Vitetti, G.: Sulla presenza del germe del morbillo nell' essudato naso-faringeo, ibid. **32**:781 (July 1) 1924. Auricchio: Ricerche sulla etiologia del morbillo, Riv. di clin. pediat. **22**:729, 1924. Pacchioni, D.: Ricerche bateriologiche nel morbillo, Atti. d. Accad. med.-fis. fiorent., 1903, p. 33. Salvioli, G.: Ricerche sul virus morbilloso de Caronia, Pediatria **33**:737, 1925.

14. Ritossa, P.: Reperto del germe del morbillo in uno nato—morto da madre morbillosa, Pediatria **32**:513 (May 1) 1924; Reazioni serologiche nell' infezione morbillosa, ibid **32**:784 (July 1) 1924; abstr., J. A. M. A. **83**:649 (Aug. 23) 1924.

15. De Villa, S.: L'intradermoreazione ned morbillo, Pediatria **32**:769 (July 1) 1924.

vaccine, no reaction was produced. The same observation was made by Rapisardi,[16] who employed the same technic among newly born and very young infants. Hecht,[17] in Germany, is skeptical of these reactions.

One of the notable aspects of the work of Caronia and his associates is the production of antimorbillous vaccine with which they claim to have succeeded in establishing methods of passive and active immunization. The basis of this vaccine production was the observation by Caronia of the fact that when he had injected phenolytic cultures of his organism into well infants who had never had measles, they were found to be refractory to the disease on repeated exposures at later time. Moreover, these children were immune even when their throats were painted with the nasopharyngeal secretions from patients with active measles. Encouraged by these results, he prepared a vaccine with self-developed cultures phenolized to 0.5 for 100. This he injected intramuscularly in 2 cc. quantities at a time on alternate days. It was found that three injections of this vaccine were not sufficient, and it often required as many as five for complete protection. He found that immunization was slow and feeble in persons suffering from tuberculosis or syphilis.

The method of antimorbillous vaccination was subjected to a rather extensive study and trial by Sindoni,[18] who found that of the 346 children who received from three to five injections of 2 cc. each of Caronia's vaccine intramuscularly every second day, only one child developed measles. This great success was due to an early administration of vaccine, for in another asylum where vaccination was employed late, 80 per cent of the children developed the disease. In 60 cases of vaccination in private homes, the protection was complete, while in a hospital, of 133 children who were vaccinated, 8 developed the disease. Satisfactory results are also reported by Ricciardi,[19] Aunecchino,[20] Szirmai and Jacobovics,[21] and Emmanuella,[22] while unfavorable comments are made by Redlich,[23] Nobel and Schönberger,[24] and Nobel.[25]

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16. Rapisardi, S.: Sulla recettivita del neonato e del lattante per l'infezione morbillosa, Pediatria **32**:1271 (Nov. 1) 1924.

17. Hecht, A. F.: Intradermoreactions with Caronia's Scarlet Fever and Measle Toxin, Ztschr f. Kinderh. **40**:309, 1925.

18. Sindoni, M. B.: Sulla vaccinoprofilassi del morbillo, Pediatria **33**:173, 1925; Presse méd. **75**:1255 (Sept. 19) 1925.

19. Ricciardi, L.: La vaccino-profilassi anti-morbillosa nella practica ospedaliera, Pediatria **33**:1333, 1925.

20. Aunecchino, P.: Vaccino-profilassi de morbillo, Pediatria **33**:1006, 1925.

21. Szirmai, F., and Jacobovics, B.: Experimentelle Untersuchungen zur Frage der Aetiologie des Scharlachs und der Masern, Jahrb. f. Kinderh. **111**:331 (Feb.) 1922; abstr., J. A. M. A. **86**:1406 (May 1) 1926.

22. Emmanuella, A.: Risultati della vaccinoprofilassi antimorbillosa nell'asilo Vittorio Emmanuelle III di Napoli, Pediatria **34**:30 (Jan. 1) 1926.

Caronia [26] reported also successful attempts to produce experimental measles in young rabbits by the injection of blood or filtrates of nasal secretions taken from patients during the height of the rash as well as by the injection of cultures of the isolated organism. Experimental inoculation by using Caronia's organism is also reported by Belot and Moureau [27] and Laurinsich.[28]

The work of Caronia in Italy has since been confirmed by Arloing and Dufourt [29] in France and by Torello Cendra [30] in Spain, but in Germany, England and the United States, little reference is made to his work, while Takaki [31] of Japan has completely failed to get the same results by following Caronia's method. Recently, Langley Porter [32] of San Francisco has made a complete review of the Italian literature, and its importance has been brought to the attention of the American medical profession.

Much as yet cannot be said of the discovery of a streptococcus of measles isolated by Ferry and Fisher [33] of Detroit in 1926, as there has been no confirmation of their results other than their own research. The morphologic and cultural characteristics of this organism are given as follows:

It is a medium-sized, gram-positive, aerobic streptococcus, occurring in long chains in liquid medium and in chains of varying length on solid medium, which

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23. Redlich, Fr.: Ueber Scharlach- und Masern-prophylaxe nach Caronia, Seuchenbekämpfung, no. 6, 1925; cited by Gröer and Redlich: Ergebn. d. inn. Med. u. Kinderh. **30**:506, 1926.

24. Nobel, E., and Schönberger, M.: Ueber die Masernprophylaxe nach Caronia, Ztschr. f. Kinderh. **40**:197, 1925.

25. Nobel, E.: Prevention of Measles, Monatschr. f. Kinderh. **31**:275, 1926.

26. Caronia, G.: Sul morbillo sperimentale, Rinascenze medica, 1924.

27. Belot, J., and Moureau, M.: Recherches sur l'étiologie de la rougeole. Études bactériologiques et expérimentales du microbe de Caronia, Soc. méd. et chir. de Bordeaux, July 18, 1924, J. de méd. de Bordeaux et du Sud-Ouest **101**:675 (Aug. 10) 1924.

28. Laurinsich, A.: Sul morbillo sperimentale, Pediatria **32**:772 (July 1) 1924.

29. Arloing, F., and Dufourt, A.: Recherches sur l'étiologie de la rougeole. Culture du microbe de Caronia, Compt. rend. Soc. de biol. **90**:763 (March 28) 1924.

30. Torello Cendra, M.: Edutie acerca del coco de Caronia, Rev. espan. de med. y cir., 1924, cited by Pollitzer, R.: Presse méd. **33**:1269 (Sept. 23) 1925.

31. Takaki, J.: Cultivation of Virus of Measles and Scarlet Fever According to Caronia's Method, J. A. M. A. **86**:1669 (May 22) 1926.

32. Porter, L.: Scarlet Fever and Measles: Review of Recent Italian Literature, Arch. Pediat. **43**:197 (March) 1926.

33. Ferry, N. S., and Fisher, L. W.: Measles Toxin: Its Preparation and Application as a Skin Test, as an Immunizing Agent, and for the Production of an Antitoxin, J. A. M. A. **86**:932 (March 27) 1926. Ferry, N. S.: Etiology of Measles, Am. J. Pub. Health **17**:565 (June) 1927; Etiology and Pathogenesis of Measles, J. Med. **8**:191 (June) 1927.

produces a small colony with a green halo on whole blood agar. It does not produce hemolysis of red cells, is not soluble in bile, and does not liquefy gelatin. It ferments glucose, lactose and saccharose, and does not ferment mannite, salicin, or inulin. It is characterized by its production of an extracellular toxin specific to measles.

They claim that their organism differs from that described by Tunnicliff, chiefly because it grows rather luxuriantly in aerobic conditions, and they have named this organism *"Streptococcus morbilli,* Ferry." In many respects, however, both morphologic and cultural, their streptococcus "appearing in pairs" resembles the diplococcus discovered by Tunnicliff exactly nine years previously. These authors found this organism uniformly present in the blood of patients with measles during the early stages of the disease, and that it elaborates a soluble toxin which gives specific skin reactions in persons who are not immune to measles, this reaction being absent in those known to be immune to measles or when the organism is injected together with either the measles convalescent serum or the serum of an animal immunized with the measles toxin. The subcutaneous or intracutaneous injection of measles streptococcus into rabbits is characterized by local reactions associated with a generalized rash and conjunctival congestion.

The coccus theory of the etiology of measles at present appears to be the most promising, although there are certain glaring failures to confirm the presence of such a coccus even under the most accurate and rigid scientific control. Thus, Long and Cornwell [34] in Boston completely failed to obtain any cultures from twenty-six patients with measles other than occasional scanty growths which they believe to be the result of contamination. The studies on the measles coccus are still in progress; in order to establish its etiologic relationship, the Koch's postulates must be fulfilled, including the more successful demonstration of human inoculation.

In contrast with the foregoing theory, there still exist a number of workers who believe the cause of measles to be some form of filtrable virus. Thus Park [35] of New York thinks that the incubation period of measles is too long for a bacteria of streptococcus group. Degkwitz,[36] in support of a filtrable virus theory, brings forth experimental evidence to the effect that the filtrate of cultures which is bacteriologically sterile can adequately cause measles when inoculated into man and animals.

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34. Long, P. H., and Cornwell, A. M.: Observations on the Etiology of Measles, J. Infect. Dis. **40**:408 (March) 1927.

35. Park, W. H., in a discussion of paper by Cary and Day: Etiology of Measles, J. A. M. A. **89**:1208 (Oct. 8) 1927. Park, W. H.; Williams, A. W., and Wilson, M.: The Relation of Tunnicliff and Ferry Diplococci to Measles, Am. J. Pub. Health **17**:460 (May) 1927.

36. Degkwitz, R.: Etiology of Measles, J. Infect. Dis **41**:304 (July) 1927.

According to his experience, the virus of measles can be kept alive for several weeks outside the human system, if blood from patients with measles is drawn just at the beginning of the rash and diluted in the proportion of from 1:7 to 1:10 with buffered salt solution containing the same number of anions and kations and showing the same p_H as blood. This mixture must be kept at a temperature of 0 C. He found that the specificity of reactions from measles provoked in human beings with sterile filtrates of cultures can be proved by the fact that such persons are later immune against large amounts of infectious blood. Scott and Simon [37] likewise considered the causative agent of measles to be some sort of filtrable virus, as their summary of observations describes only the nature of the virus, the mere shadow of the organism, without catching the reality. Caronia does not give up the possibility of a filtrable virus as being the cause of measles when he says that his microbe "passes through ultramicroscopic phase in the cycle of development." On the whole, however, it may be concluded that to advance a filtrable virus theory of the disease is merely to acknowledge the inability to discover the organism, for a virus is nothing but a toxin which has its origin in the bacteria. As more advanced knowledge of bacteriology is gained, the term virus will be gradually eliminated from the scientific vocabulary.

EXPERIMENTAL INOCULATION IN MAN

As early as 1755, Brown [38] expressed the idea that by first laying a piece of wool or wood on the measles eruptions and transferring it to the healthy skin of a susceptible person, inoculation might be accomplished. Two years later, Alexander Monro [39] modified Brown's suggestion by bringing out the point that "it is probable that inoculation can be performed, if only the pustules and spots of matter can be rubbed on cotton, and if this (either fresh or put on glass carefully covered and preserved) be applied to a little wound, exactly in the same way as variolous matter." On the suggestions of these two writers, Francis Home [40] of Edinburgh attempted inoculations in fifteen children, and

37. Scott, J. M., and Simon, C. E.: Experimental Measles; Fate of Measles Virus in Inoculated Rabbit and Its Viability Outside of Body, Am. J. Hyg. **5**:109 (Jan.) 1925.

38. Brown, Carl: Dissertatio medica inauguralis de morbillis, Edinburgh, 1775.

39. Monro, Alexander (Secundus): De venis lymphaticis vavulosis et de earum in primis origin, 1757.

40. Home, Francis: Medical Facts and Experiments, Edinburgh, 1759. The quotation is taken from Hektoen: J. Infect. Dis. **2**:238, 1905. Dickson's reference to a certain "Fr. Herne" who made the first experimental inoculation in France is due to typographical error. Pétges and Gadaud: J. méd. de Bordeaux et du Sud-Ouest **103**:573 (July 10) 1926. Dickson, E. C.: California & West. Med. **26**:345 (March) 1927.

published a rather careful record of his work. His method reads in part as follows:

> I applied directly to the magazine of all epidemic diseases, the blood. As the measly matter behoved to be but a small portion of the whole mass, I choose to make use of the blood when it contained the morbific matter in the highest state of acrimony. In that situation the blood seemed to me to be, the next day after the turn of the measles, when their matter by juxtaposition and stagnation becoming more acrid, as we know happens in all eruptive cases, was again absorbed into the mass of the blood, and was the cause of the inflammations which happened then and afterwards. I chose to take it from the most feverish patients. . . . I ordered a very superficial incision to be made amongst the thickest of the measles, and the blood which came slowly away was received upon some cotton. What I had most to fear was a deficiency of morbillious matter; and, therefore, it was plain, that the sooner it was applied, and the more close it was kept, the better chance it had to succeed. An incision in each arm, as is made in the smallpox, was giving it a greater opportunity to take place. I thought it a very material point to allow the wounds to bleed for a quarter of an hour before the cotton was put in, that the fresh blood might not wash off, or too much dilute the morbillious matter. I have always let it remain three days in the wound. I have kept exactly to all these circumstances, finding that the observance of them was attended with success.

Home summarized the results of his experiments in a table which is complete in many respects. The most significant point in the data which he set forth in this table is the incubation period of inoculated measles. This period varied from three to eleven days. Of the nine patients who were inoculated successfully, four showed the incubation of seven days, while the other five showed the variable numbers of three, four, six, eight and nine days. He commented on this point as follows: "In the inoculated measles the patient generally sickens about the 6th day. Here the disease comes on sooner and seems to be more fixed in the time than in the inoculated smallpox, which varies from the 7th to the 10th." Whether or not the experimental measles has a shorter incubation period than the natural infection, remains to be seen. Some later investigations seem to point to the fact that it is the same in both forms of the disease, as we shall see later. Again, Home gave no account of the care he should have exercised in excluding spontaneous and natural infection in his experiment.

At any rate, Home's experiment was heralded by the press as highly significant. The following paragraph appeared in *The Gentleman's Magazine* in 1758:

> Historical chronicle, June, 1758. Tuesday 23. A discovery of the highest utility has lately been made at Edinburgh, and already sufficiently confirmed by a number of successful experiments: Dr. Francis Home has inoculated for the measles, and has produced a disease free from all alarming symptoms.[41]

41. Home: The Gentleman's Magazine & Historical Chronicle **28**:285, 1758.

TABLE 2.—*Chronological List of Original Reports on Human Inoculations*

Author and Source	Method of Inoculation	Number of Cases	Results
Home, Francis: Medical Facts and Experiments, 1758	Blood soaked cotton placed on incised forearm for 3 days	15	Positive results in 9, negative in 6
Green (1799), quoted by Stewart, J.: A Practical Treatise on the Diseases of Children, 1844, p. 416	Blood in grave measles	3	Successful
Wachsel (1801), quoted by Willan: On Cutaneous Diseases, 1809, vol. 1, p. 106	Fluid taken from measly vesicles	1	Eruption on the 22d day after inoculation
Chapman (1801), quoted by Dewes: A Treatise on the Physical and Medical Treatment of Children, 1858, p. 439	Blood, tears, nasal mucus, and eruptive matter of cuticle, properly moistened	..	No effect
Rasori (1806), cited by Speranza, quoted from Hektoen	Eruptive skin	1	Formation of papule at point of inoculation
Willan, R.: On Cutaneous Diseases, 1809, vol. 1, p. 106	Fluid from miliary vesicles	3	Unsuccessful
Themmen, C. J.: Diss. Med. Inaug. Histor. epidem. Morbillosae, Groningae, 1816	Blood, tears and perspiration	5	No effect
Speranza (Mantua): Storia del morbillo epid. della provincia di Mantova, 1824	Bloody matter from skin, using vaccination method	6	No typical result
Negri, cited by Speranza, 1824	Home's method	2	No effect
Albers, J. F. H.: Jahrb. Chir. u. Augenh. **21**: 541, 1834	Blood, using both Home's method and that of vaccination	4	Without success
Katona, von: Oesterr- med. Wchnschr. **1**: 1, 1842	Vaccination method with tissue fluid taken at height of fever	1122	Positive in 93%, eruption appearing from 9 to 10 days
McGirr, J. E.: Northwest. M. & S. J. **7**: 434, 1850	Blood inserted into the arm	3	Measles rash appeared on 4th, 6th and 7th days
Mayr, F.: Ztschr. d. kais.-kon. Gesellsch. d. Aerzt zu Wien **8**: 15, 1852	Subcutaneous injection of materials from early papules	6	Eruption on 14th day
	Use of nasal secretions	2	Rash on 8th-9th day
	Desquamating epithelium	..	No effect
Bufalini: Rev. Scient. della R. Academ. de Fisiocritici **1**: 111-125, 1839	Combination of Home's and Speranza's methods	6	Positive results in 4 and negative in 2
Thomson, Hugh: Glasgow Med. J. **33**: 420, 1890	Blister fluid	2	Slight catarrh, but no rash
Hektoen, L.: J. Infect. Dis. **2**: 238, 1905	4 to 5 cc. of 24 hour culture of infected blood in ascites broth, injected subcutaneously	2	Eruption on 14th day in both cases, one of which showed no catarrhal signs
Herrman, C.: Arch. Pediat. **32**: 503, 1915	Nasopharyngeal swabs, collected 24 hours before eruption	40	Rise of temperature in 15 on 14th day, with indistinct rash
Sellards, A. W.: Bull. Johns Hopkins Hosp. **30**: 257, 1919; **30**: 311, 1919	Blood, following Hektoen's method	2	No effect
Richardson and Connor: J. A. M. A. **72**: 1046 (April 12) 1919	Nasopharyngeal swabs obtained on first day of rash, inoculated together with immune serum	3	In one case, rise of temperature with atypical rash
Caronia, G.: Pediatria **31**: 801, 1923	Large and repeated doses of recent cultures of Caronia's organism intramuscularly	3	Attenuated form of measles with catarrh and rash on 12th-13th day
Degkwitz, R.: J. Infect. Dis. **41**: 304, 1927	1 cc. of infective blood carried through generations in dilutions of 1:7-1:10	3	Positive results

Again, J. Cook [42] wrote in the same magazine several years later as follows:

I would therefore beg leave to recommend to the public the practice of inoculation in this distemper (measles) as well as in the other (smallpox), and am confident that by this method many may be preserved from the malignant sort which ofter proves mortal, and is always dangerous.

Dr. Francis Home was the first who attempted this practice at Edinburgh about nine years ago, since which, many physicians in that country have followed his example, though I do not find it is much encouraged in England, though in smallpox it is now become universal.

The method is easy: Dip a little bit of cotton or lint, on the watery humour that stands in the eyes of persons ill of the measles about the time of the crisis, make a slight scratch in the arm, above the elbow, of the person to be inoculated, put the watery pledget upon the incision and cover it with a bit of sticking plaster to keep it on; and this without further trouble will produce the measles in a gentle and favorable degree, which, during the whole course, will want no other care than that of keeping the patient moderately warm, nor any attendance but that of watching the fever, and encouraging the crisis, which, in a few days will carry off the infection, and complete the cure. This epidemic disease should be communicated to those young subjects who have not yet had it, when it makes its first appearance in any neighborhood, by which the dangerous symptoms that often attend it will be effectually prevented.

The practice was further recommended by Spry,[43] who gives a modification of the method of inoculation as follows:

The method of procedure in inoculating for measles does not differ from that which is to be followed in the case of smallpox. I think there is only one thing which in this case deserves notice as being peculiar, viz., that the linen threads which are used for introducing the contagion ought to be impregnated with blood, for matter is rarely found, drawn from the pustules of the measles near the tip or a little way from it.

In this method of treatment, not yet so common as the earlier one, all the symptoms are found to be less serious—a fact of which I am quite certain, not from one observation, but from the study of many cases.

Whether or not inoculation for measles, following the suggestion of these early writers, became a universal practice, is not definitely known. The report of Home's experiments, however, aroused a wide interest in the subject, and a number of critics appeared who either lauded or severly criticized the researches of Home. Buchner,[44] Nils Rosen von Rosenstein [45] and Holst [46] are among those who highly

42. Cook, J.: The Gentleman's Magazine & Historical Chronicle **37**:163, 1767.

43. Spry, E.: De variolis ac morbillis iisque inoculandis, 1768; cited by Hektoen.

44. Buchner, quoted by H. Zeiss: Ergebn. d. inn. Med. **20**:4, 1921; also cited by Hektoen.

45. Rosen von Rosenstein, Nils: Anweisung zur Kenntniss und Kur der Kinderkrankenheiten, ed. 4, Göttingen, 1781, p. 322.

46. Holst, quoted by Hektoen.

praised Home's work. Vogel,[47] the senior, remarked wisely: "Insitio morbillorum posset omnino in pestiferis epidemiis suum usum habere." Vogel,[48] junior, said that Home's example was followed by several physicians in Scotland, but sufficient data were not available, and, although inoculation for measles had not the same significance as vaccination for smallpox, yet the practice could be recommended if a severe epidemic of measles existed in the neighborhood.

On the other hand, many critics offered adverse words about Home's experiment, and some even doubted the genuineness of his records. In his widely read textbook Borsieri (Burserius)[49] of the University of Pavia, disposed of Home's research by saying, "Nihilo tamen minus morbillorum insitio pancos admodum sectatores habuit sic ut pene iam desueverit." Cullen,[50] who was Home's contemporary and colleague, did not mention inoculation for measles, and in the German edition of the same book, the translator inserted an annotation to the effect that inoculation had never become popular. Thomas[51] (1815) and Ronalds (1816) remarked that Home's attempts were made only on a small scale, and it was not certain that the disease was always benign. The criticisms offered by Thomassen a Thuessink[52] and his pupil, Themmen,[53] are fully reviewed by Hektoen. Albers expressed the opinion that since Home's work had been done in a hospital continuously occupied by patients with measles, the infection might have arisen in some other way. Jörg and also Wendt, according to Thomas,[54] asserted that the measles from inoculation did not run a lighter course in any case, and declared these therefore as useless. The most conclusive invective against the credibility of Home's inoculations was offered by Hektoen,[55] who, after a painstaking review of the literature directly related to the researches of Home, said:

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47. Vogel, R. A.: Academicae praelectiones de cognoscendis et curandis praecipuis corporis humanis affectibus, Göttingen, 1777, p. 99.

48. Vogel, S. G.: Handbuch der praktische Arzneywissenschaft zum Gebrauch für angehende Aerzte, Stendal, 1795, pt. 3, pp. 216-219.

49. Burserius, J.: Institutionum med. pract. quas auditoribus suis praelegebat, Leipzig, 1787, p. 2.

50. Cullen, William: First Lines of the Practice of Physic, for the Use of Students in the University of Edinburgh, ed. 2, 1778, vol. 1, p. 211.

51. Thomas, Robert: The Modern Practice of Physic, American ed. 3 from English ed. 4, 1815, p. 223.

52. Thomassen a Thuessink: Abhandlungen über die Masern, Göttingen, 1830, p. 162.

53. Themmen, C. J.: Dissertatio medica inauguralis historiam epidemiae morbillosae, Groningae, 1816.

54. Thomas, L., in Ziemssen: Cyclopedia of Practical Medicine, 1875, vol. 2, p. 40.

55. Hektoen, L.: Experimental Measles, J. Infect. Dis. **2**:238, 1905.

> Examination of this table cannot but lead to the conclusion that probably not a single one of the fifteen cases inoculated by Home had measles as a result of the inoculation. . . . His records show that in no case was the time between the inoculation and the supposed measles rash, which is not described in detail, more than 10 days. . . . On the whole there seems to be no escape from the conclusion that Home's claim to have produced measles by inoculation is without foundation.

Be that as it may, Home's experiment furnished an impetus sufficiently powerful to cause investigators to make a number of experimental inoculations in man, as cited by Hektoen, namely, Locatelli, Rossi (Rasori?), Frigeri (Frigori), Horst (Holst), Percival, Giotanna (Girtanner), Vaidy and Fellegen (Tellegen), although the sources of these researches are not available, and therefore cannot be reviewed. The authentic inoculations have been tabulated in table 2, which helps to show both the successful and unsuccessful production of measles in man by inoculation. In many of the so-called successful cases, no adequate precaution is taken to exclude natural infection, and a large number of these original articles are lacking in detail in descriptions of methods.

The first accurately controlled experiments were made by Hektoen in 1905, who, after reviewing in detail all reports of experimental inoculation in man, recorded two cases of successful production of measles in persons. In the first case, he took 3 cc. of blood from a patient with measles on the first day of the rash and mixed it with 50 cc. of ascites broth, and after an incubation of twenty-four hours, at 37 C., 4 cc. of this mixture was injected subcutaneously. In the second case, 2.5 cc. of blood from a patient with measles, taken about thirty hours after the first appearance of the rash, was mixed with 75 cc. of ascites broth, and after an incubation of twenty-four hours at 37 C., 5 cc. of this mixture was injected subcutaneously. In both cases the inoculated broth remained sterile, the culture being kept under aerobic conditions. In both cases there was a febrile reaction on the thirteenth and eleventh day, respectively, followed by a typical measles rash appearing on the fourteenth day after inoculation, although in the first case, it was a type of the disease known as "morbillo sine catarrho."

Herrman's attempt at active immunization by inoculating infants under 5 months of age with a cotton swab which had previously been rubbed against the mucous membrane of patients afflicted with measles resulted in producing a rise in temperature and a few morbillous spots on the skin in from fourteen to eighteen days. Whether this may be interpreted as being a successful inoculation of human beings is difficult to say, but Herrman's attempt stands as an interesting landmark in the history of inoculations into man as well as of that of active immunization. The same may be said of the three cases reported by Richardson and

Connor of Providence in 1919. In 1923, Caronia inoculated into three children large and repeated doses of recent cultures of his organism, injecting them intramuscularly, and in from twelve to thirteen days an attenuated form of the disease with catarrh and rash developed in all cases. More recently, Degkwitz claimed to have produced typical measles with the blood of a patient with measles, which was bacteriologically sterile, in proper dilutions, after having passed it through a Berkefeld filter.

In this connection an interesting observation coming from the Minneapolis General Hospital, reported by Bauguess,[56] may be of value in throwing further light on the nature of inoculation into man. He reported two cases in infants, aged 3 and 9 months, who received blood transfusions from their own mothers for extreme degrees of malnutrition. The blood in both cases was withdrawn from mothers who appeared to be in good health; it was citrated and given in amounts of 60 and 75 cc., respectively. Measles rash developed in the older baby on the thirteenth day after transfusion and in the younger on the fourteenth day. On careful investigations, both mothers were found to have developed measles eruption two days after transfusion.

From the foregoing instances of inoculation into man, both experimental and accidental, it may be said in summary that in spite of a certain number of failures, the disease can be inoculated experimentally under proper conditions into human beings by means of blood and nasopharyngeal secretions. It must be remembered, however, that the inoculated disease differs somewhat from the original one in almost all cases and is never typical of clinical measles; it is usually designated as being a form of attenuated or modified measles. As I shall review in later paragraphs, the production of an attenuated form of the disease is advocated by some writers as the method of choice in establishing the type of immunity which lasts as long as that conferred by natural contact.

EXPERIMENTAL INOCULATION IN ANIMALS

As early as in 1774, Brinckmann[57] remarked that the virus which sets up pathologic symptoms in human beings can produce the same effect in animals. His statement was probably based on a rather significant demonstration of the susceptibility of animals to measles as recorded by M. Paulet of Paris. In 1770, according to the *Gazette Salutaire*, Paulet[58] made the following observation: A monkey, perhaps in his

56. Bauguess, H.: Measles Transmitted by Blood Transfusion, Am. J. Dis. Child. **27**:256 (March) 1924.

57. Brinckmann, J. P.: Beiträge zu einer neuen Theorie der Gärungen, Düsseldorf, 1774, vol. 8, p. 106.

58. Berlinische Sammlungen: Betrachtungen aus einem Briefe des Herrn Paulet von einem Affen der die Masern oder Rötheln bekommen **5**:174, 1773.

possession, was allowed to lie for a long time in the same bed as that occupied by a young child who was infected with measles. To the surprise of every one, the animal came down with measles with all the customary signs of cough, convulsions of limbs, malaise, vomiting, redness of eyelids, sparkling eyes and heavy tongue; by the end of another day, there were eruptions on the face and on the upper portion of the body not covered by hair which left no doubt as to the nature of the disease. The eruption on the face was discrete, numbering about fifty lesions; in three days they were transformed into small spots, and all symptoms had subsided.

As to measles in domestic animals, especially in sheep and swine, there are numerous descriptions by older veterinary writers, as reviewed by Geissler,[59] but it is problematic whether the disease they were observing was true measles. Chisholm[60] described a case of measles in a dog, but there is no record of a rash. King[61] advanced a theory as to the presence of measles virus in mice, but he did not give definite evidence. Winkler[62] imagined that measles came from swine, a fact which entirely lacks foundation, while Krautheim[63] seems to have erred in his diagnosis of erysipelas in swine as measles.

The first authentic inoculation of measles into experimental animals was performed by Behla,[64] who placed warm nasal mucus and saliva from patients with measles on the nasal and buccal mucous membrane of rabbits, guinea-pigs, cats, mice, dogs and lambs, but the results were indefinite except for the presence of catarrhal symptoms. He then took a pig, 6 weeks of age, and rubbed fresh warm nasal and oral mucus removed from a patient with measles at the height of the eruption on the corresponding mucous membrane of this animal. In order to insure the implantation of the virus, he scratched the mucous membrane of the pig with a sharp needle. Rhinitis and conjunctivitis developed on the fourth day, accompanied by anorexia and fever. On the eighth day, a rash began to appear on the face, especially near the proboscis and ears, and on the inner aspects of both front feet; within twenty-four hours this rash spread over the whole body. On the following day, it faded and desquamation was evident. Two weeks later, the second

59. Geissler, E. A.: Bern Diss., 1903.

60. Chisholm, J. J.: A Case of Measles, Followed by Deafness, in a Dog, Contracted from a Human Subject, M. Rec. **35**:126, 1886.

61. King, A. F. A.: Measles and Mice (Does the Microbe of Measles Come from Mouse?), Washington M. Ann. **9**:49, 1910.

62. Winkler: Wchnschr. f. Tierh. u. Viehzucht. **36**:162, 1892.

63. Krautheim: Masernexanthem bei Schweinen, Wchnschr. f. Tierh. u. Viehzucht. **36**:438, 1892.

64. Behla, R.: Der Erreger der Klauen- und Maulseuche nebst Bemerkungen über die akuten Exanthem beim Menschen, Centralbl. f. Bakteriol **13**:50, 1893; **13**:87, 1893; Ueber das Vorkommen von Masern bei Tieren, ibid. **20**:561, 1896.

older hog became ill with measles, while still a week later the third animal developed the same signs of measles; Behla concluded that this was due to contact with the first pig. Similar inoculation experiments reported by Warschawsky [65] and Pomjalowsky [66] were attended by failure. This led Josias [67] in 1897 once more to undertake experimental inoculation of measles into swine. All of his ten hogs that were inoculated in the same way as those of Behla gave negative results, which forced Josias to suggest that Behla may have encountered eruptive diseases natural to hogs instead of measles inoculated from human subjects.

By far the greatest number of experiments on animal inoculation has been made with various species of lower monkeys, and it is with these monkeys that one can get the most illuminating facts as to the nature of measles infection. The first attempt was that of Josias; he was inspired by the experience of Chavigny who, in 1898, noted that a monkey (*Macacus cyanocephalus*) fell ill with measles eight days after its keeper developed a rash, while the other monkey (*Macacus cercopithicus*) attended by the same keeper remained unaffected. Josias took the nasopharyngeal secretion in the early eruptive period and rubbed it over the mucous membrane of the nose and throat in some animals, while in others he injected subcutaneously from 0.5 to 1 cc. of blood, from subjects with measles. In five rhesus monkeys a reaction was not seen, but in three sajous monkeys, a typical exanthem developed. Josias concluded that the rhesus monkeys are thus refractory to measles while the sajous are not.

In Great Britain, Grünbaum published a report of a rather indefinite result in a chimpanzee from Zanzibar following the injection of blood from subjects with measles, which led him to conclude that he had probably conferred immunity on the animal rather than transmitted the disease.

The most important work on measles in monkeys was done by Anderson and Goldberger,[68] who in a series of papers showed that at

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65. Warschawsky, W. M.: Zur Aetiologie und klinische Bakteriologie von Masern und deren Komplikationen, Dissertation, 1895; cited by Jurgelunas: Centralbl. f. Bakteriol. **72**:483, 1914.

66. Pomjalowsky: Das Masernbakterium und das Anti-Masernserum; cited also by Jurgelunas (footnote 65).

67. Josias, A.: Recherches experimentales sur la transmissibilité de la rougeole, Tribune méd. **30**:211, 1898.

68. Anderson, A. F., and Goldberger, J.: Experimental Measles in Monkey: A Preliminary Note, Pub. Health Rep. **26**:847 (June 9) 1911; A Supplementary Note, ibid. **26**:887 (June 16) 1911; The Period of Infectivity of the Blood in Measles, J. A. M. A. **57**:113 (July 8) 1911; The Nature of Virus of Measles, ibid. **57**:971 (Sept. 16) 1911; The Infectivity of the Secretions and the Desquamating Scales of Measles, ibid. **57**:1612 (Nov. 11) 1911; Recent Advances in Our

(Footnote continued on page 550)

TABLE 3.—*Chronological List of Reports on Animal Inoculations*

Author and Source	Number of Animals	Method	Result
Behla, R.: Zentralbl. f. Bakteriol. **13**: 50, 1893; **13**: 87, 1893; **20**: 561, 1896	Rabbits, guinea-pigs cats, lambs, mice, dogs,	Placing warm nasal mucus and saliva from patient with measles	Indefinite catarrhal signs
	1 to 6 week old pig	Applied warm mucus on scratched mucous membrane	Catarrh on 4th day, rash on 8th day, followed by scaling
Chavigny, P.: Bull. méd. Paris **12**: 334, 1898	Mac. cyanocephalus	Natural contact	Catarrh on 8th day, rash on 14th day
	Mac. cercopithecus	Remained well throughout	
Josias, A.: Méd. mod. **19**: 153, 1898; Bull. méd. **12**: 230, 1898; Tribune méd. **30**: 211, 1898	5 Mac. rhesus, 3 Sajou robustus	Application of nasopharyngeal mucus; subcutaneous injection of blood and mucus	No reaction; catarrh and rash, with desquamation
Warschawsky (1898) cited by Jurgelunas	5 pigs and rabbits, Mac. rhesus	Blood intravenously, subcutaneously and intraperitoneally	No results
Lesage, M.: Compt. rend. Soc. de biol. **52**: 203, 1900	Puppies	Blood and mucus	Septicemia developed but no measles
Geissler, E. A.: Bern Diss., 1903	3 sheep and swine, 2 goat cat, 4 dogs	Mucus, crusts and scales, applied in various ways	Only local changes, and slight catarrh; no rash
Grünbaum, A. S.: Brit. M. J. **1**: 817 (April 9) 1904	2 chimpanzees	Injection of blood, application of mucus, and clothing of patient with measles	No reaction
Zlatogoroff, S. J.: Centralbl. f. Bakteriol. **37**: 249, 1904	Albino mice, puppies, guinea-pigs	Blood	No reaction in some; others died in 12 to 14 days
Pomjalowsky (1906), cited by Jurgelunas	Guinea-pigs, puppies and hogs	Blood subcutaneously and intravenously	No reaction
Anderson, J. F., and Goldberger, J.: Pub. Health Rep. **26**: 847, 1911; **26**: 887, 1911	Mac. rhesus, Mac. cynomolgus, Mac. sinicus	2 to 3 cc. of defibrinated blood, intraperitoneally, subdurally and intracardially	Positive results in almost 50 per cent of cases
Hektoen, L., and Eggers, H. E.: J. A. M. A. **57**: 1883 (Dec. 2) 1911	2 Mac. rhesus	Citrated blood drawn 24 hours after rash	Malaise in 12 days, rash on 15th day, with leukopenia
Nicolle, C., and Conseil, E.: Compt. rend. de Acad. Sc. **153**: 150, 1911	1 M. sinicus	Blood intraperitoneally	Fever on 9th to 12th day; no rash
	Rabbits, guinea-pigs	.....	No reaction
Tunnicliff, R.: J. Infect. Dis. **11**: 474, 1912	Mac. rhesus	Blood	A protracted leukopenia for 15 days, but no other reactions
Lucas, W. P., and Prizer, E. L.: J. Med. Research, **26**: 181, 1912-1913	2 Mac. rhesus	Measles serum and serum with corpuscles	Leukopenia and Koplik spots on 10th day, but only transient erythema
	Mac. rhesus	Subinoculation	
Götze, E.: Jahrb. f. Kinderh. **76**: 205, 1912	10 weeks' old hog	Defibrinated blood (1 cc.) intravenously	Fever on 19th day, with rash on ears
Jurgelunas, A.: Russk. Vrach no. 32; Centralbl. f. Bakteriol. **72**: 483, 1914	1 pavian, 1 Mac. cynomolgus, 1 Mac. rhesus, rabbits and pigs	5 cc. defibrinated blood intravenously	Sick on 10th day with catarrh and rash, but no fever; negative
Hlava: Centralbl. f. Bakteriol. **63**: 270, 1915	Mice, rats, rabbits and guinea-pigs	Secretions of respiratory tract; also scales	No effect
	Monkeys	Subcutaneous and intratesticular injection	Positive results
Sellards, A. W., and Wentworth, J. A.: Bull. Johns Hopkins Hosp. **30**: 57, 1919; **30**: 311, 1919	3 Mac. rhesus	Diluted and defibrinated blood injected intraperitoneally	No results, except in one in which slight rash before incubation period
	2 monkeys	Blood	Leukopenia on 6th to 9th day, rash on 12th day, but no fever

TABLE 3.—*Chronological List of Reports on Animal Inoculations—Continued*

Author and Source	Number of Animals	Method	Result
	2 Mac. syrictus 2 Mac. rhesus	Conjunctival mucus Conjunctival and nasal secretion rubbed on scarified mucous membrane	Negative Negative
Nicolle, C., and Conseil, E.: Compt. rend. soc. de. biol. **83**: 56, 1920	1 Mac. sinicus 2 Mac. sinicus 1 Mac. sinicus	Blood (8 cc.) Blood from above Blood intratesticularly	Incubation 9 days, fever on 10th day
	Guinea-pigs, swine and newborn kitten	Blood intraperitoneally	No result
Blake, F. G., and Trask, J. D.: J. Exper. Med. **33**: 385, 1921; **33**: 413, 1921; **33**: 621, 1921	10 Mac. rhesus	Intratracheal injection of large amount of salt solution of mucus	After 10 days malaise, anorexia, catarrh, Kopliks and fever; rash and leukopenia present
		Intramuscular injection of attenuated virus	A localized lesion, reinoculation proved presence of immunity
Harde, E.: Compt. rend. soc. de biol. **84**: 968, 1921	3 rabbits	1 to 2 cc. citrated measles blood intravenously	Erythema on previously shaven skin in 48 hours
Nevin, M., and Bittman, F. R.: J. Infect. Dis. **29**: 429, 1921	2 monkeys	Mucous washings intratracheally and blood	Incubation of 4 days, with leukopenia, exanthem and enanthem but no fever
Grund, M.: J. Infect. Dis. **30**: 86, 1922	23 rabbits	Intratracheal injection of 5 to 10 cc. of salt solution of nasopharyngeal washings	Slight fever, catarrh, erythema and exanthema, with leukopenia and desquamation
Kawamura, R.: Japan Med. World **2**: 31, 1922	3 Mac. fuscatus	1 cc. blood taken 60 hours before eruption	Incubation 8 to 9 days. leukopenia, rash, and catarrh; Koplik spots seen in one
	Guinea-pigs, rabbits	Subinoculation	No effect
Duval, C. W., and D'Aunoy, R.: J. Exper. Med. **35**: 257, 1922	30 (?) guinea pigs	1 to 2 cc. defibrinated blood intracardially	Fever, leukopenia in 9 to 12 days; with immunity
Ibid. **36**: 231, 1922	Rabbits	Blood intravenously, together with nasal secretions	Pyrexia, leukopenia, cutaneous reactions in 2 to 5 days and rash in 3 to 7 days
Tunnicliff, R., and Moody, W. B.: J. Infect. Dis. **31**: 382, 1922	3 monkeys, 2 guinea-pigs, 22 rabbits	Blood intravenously and intratracheally; also suspension of Tunnicliff organism	Fever and leukopenia with enanthema; exanthema in 3 of rabbits
Nevin, M., and Bittman, F. R.: J. Infect. Dis. **32**: 33, 1923	6 rabbits 4 monkeys	Blood intravenously Blood after passage through 3 to 4 rabbits	Erythema and desquamation but no fever or leukopenia in rabbits; typical signs of measles in monkeys
Caronia, G.: Presse méd. **31**: 877, 1923	Young rabbits	Contaminated blood (5 to 6 cc.) intravenously	Catarrh in 10 to 12 days and rash on 14th day
		Filtrate of nasopharyngeal secretions	Same results as with contaminated blood
		Repeated doses of culture of Caronia organism	Decrease in weight in 12 to 14 days, followed by catarrh and rash
Scott, J. M., and Simon, C. E.: Am. J. Hyg. **4**: 559, 1924	Rabbits, monkeys	Inoculation with filtrate from nasopharyngeal swabs; also blood	Fever and leukopenia with rash
Sellards, A. W., and Bigelow: Medicine **2**: 122, 1924	Monkeys	Excised skin lesion implanted on skin and mucous membrane	In one bright pink papule, 5 cm. in diameter
Purdy, W. J.: Brit. J. Exper. Path. **6**: 210, 1925	Rabbits	Blood and nasal secretions	No reaction
	2 monkeys	Used as control	Gave satisfactory reactions
Degkwitz, R.: J. Infect. Dis. **41**: 304, 1927	8 monkeys	Infectious material from measles	Positive results

least three species of the lower monkeys, namely, *Macacus rhesus, Macacus cynomolgus* and *Macacus sinicus,* are susceptible to measles, and it is probable that all monkeys are capable of taking the disease. Their method of experiment is as follows: Blood was taken from patients with measles, defibrinated and injected in amounts from 2.5 to 5 cc. into the peritoneal cavity, under the dura and into the heart. They noted as signs of positive reaction a rise in temperature, a rash on the third day after the appearance of fever, a fine branny desquamation and coryza and coughing with pneumonia. They obtained the best results with blood withdrawn just before or during the twenty-four hours immediately after the appearance of the rash, while with blood taken later the results were uncertain and after seventy-two hours, the infective power seemed to be wholly lost. Mixed nasopharyngeal secretions, diluted with salt solution and injected subcutaneously, also proved to be infective, though less so than the blood. Experiments with desquamating scales were attended with failure. A monkey that has had a definite reaction is found to be immune to a subsequent inoculation. From the results obtained by experimenting with nearly 100 monkeys, chiefly the foregoing three species, Anderson and Goldberger concluded that at least 50 per cent of the animals react in a characteristic manner. After a variable incubation period of not less than five days, there is more or less marked rise in temperature with or without catarrhal symptoms referable to the respiratory passages, such as sneezing and cough, and with or without an exanthem. Results similar to the foregoing ones were reported by Hektoen and Eggers [69] in 1911, who first made note of leukopenia analogous to that of measles in man, while the first description of Koplik spots in inoculated monkeys was made by Lucas and Prizer in 1912.[70]

Another series of well controlled experiments was undertaken by Blake and Trask [71] of the Rockefeller Institute, who inoculated monkeys intratracheally with nasopharyngeal secretions obtained by means of irrigations with salt solution in amounts sufficient to produce regurgi-

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Knowledge of Measles, Am. J. Dis. Child. **4**:20 (Jan.) 1912; Experimental Measles, Proc. Phil. Path. Soc. Trans. **14**:163, 1912; An Experimental Demonstration of the Presence of the Virus of Measles in the Mixed Buccal and Nasal Secretions, J. A. M. A. **68**:476 (Aug. 5) 1917.

69. Hektoen, L., and Eggers, H. E.: Experimental Measles in the Monkey with Special Reference to the Leukocytes, J. A. M. A. **57**:1833 (Dec. 2) 1911.

70. Lucas, W. P., and Prizer, E. L.: An Experimental Study of Measles in Monkeys, J. M. Research **26**:181 (April) 1912.

71. Blake, F. G., and Trask, J. D.: Studies on Measles: I. Susceptibility of Monkeys to the Virus of Measles, J. Exper. Med. **33**:385 (March) 1921; II. Symptomatology and Pathology in Monkeys Experimentally Infected, ibid. **33**:413 (March) 1921; III. Acquired Immunity Following Experimental Measles, ibid. **33**:621 (May) 1921.

tations. Of ten monkeys inoculated in this manner, positive results were seen in eight. The symptoms noted after from six to ten days' incubation were malaise, anorexia, catarrhal conjunctivitis, leukopenia, Koplik spots and fever. Three or four days afterward, the rash appeared, followed in from six to ten days by complete recovery. Reinoculation of the monkeys which had positive reactions previously is without effect, showing the presence of immunity, after intervals of from 12 to 254 days. Positive results are also reported by Nicolle and Conseil, Tunnicliff, Jurgelunas, Hlava, Nevin and Bittman, Kawamura *(Mac. fuscatus)*, Scott and Simon, Purdy and Degkwitz, while Warschawsky, Sellards and Wentworth and Sellards and Bigelow, report negative results.

Of smaller animals, rabbits were first used by Warschawsky, who in 1898 injected blood intravenously, subcutaneously and intraperitoneally without success. Subsequent attempts by Nicolle and Conseil (1911), by Jurgelunas (1914), by Hlava (1915), by Kawamura (1922) and by Purdy (1925) were all unsuccessful. In 1921, Harde inoculated three rabbits with from 1 to 2 cc. of blood intravenously and observed a rather intense and more or less uniform erythema appearing in forty-eight hours after inoculation and lasting for from twenty-four to forty-eight hours. The blood was withdrawn on the first day of eruption from three patients with measles and pooled with the addition of citrate. The cutaneous reaction was observed on the skin which had been shaved previous to the inoculation. The similar injection of blood from normal persons and from patients with scarlet fever gave no such results. In 1922, Grund injected intratracheally into rabbits from 5 to 10 cc. of cultures of salt solution of nasopharyngeal washings; this was followed by conjunctival inflammation, erythema, maculopapular exanthems and desquamation, with coryza, slight fever and leukopenia. In the same year Duval and Aunoy made an intravenous injection of blood together with nasal secretion into rabbits, and the animals later developed cutaneous reaction and rash, as well as fever and leukopenia. Tunnicliff and Moody injected mucous secretions intratracheally into twenty-two rabbits and produced exanthems in three cases and enanthems in the fourth. In 1923, Nevin and Bittman injected blood intravenously into six rabbits after shaving the hair, and saw the development of erythema and desquamation, but no fever or leukopenia. In 1924, Scott and Simon inoculated the filtrate from nasopharyngeal swabs and witnessed fever and leukopenia develop, but no rash. In 1923, Caronia injected contaminated blood in from 5 to 6 cc. amounts intravenously and observed catarrh in from ten to twelve days and rash on the fourteenth day.

Inoculation into sheep, goats, cats and dogs was attempted by Geissler in 1903 by using mucous crusts and scales in various ways, but he

obtained only local changes with slight catarrh, but no rash. In 1926, Tunnicliff and Hoyne reported that a goat which had previously been injected with a suspension of green-producing diplococcus of Tunnicliff produced a definite reaction with leukopenia and fever, but a rash had not been observed. Degkwitz inoculated sheep to obtain immune serum, but no details are published.

Zlatogoroff inoculated albino mice with infected blood but no reaction was seen, with the exception of the manifestations of septicemia with which some animals died in from twelve to fourteen days. Hlava's experiments with mice and rats were also failures.

First inoculation into guinea-pigs was made by Zlatogoroff in 1904, who used blood from subjects with measles, but no results were obtained. Pomjalowsky's experiments were also unfruitful, as were the attempts of Nicolle and Conseil, Hlava and Kawamura with guinea-pigs. Tunnicliff and Moody, on the other hand, obtained a rise in temperature and leukopenia in two guinea-pigs by using the blood and nasopharyngeal secretion.

The latest experimental animal used is the horse, which is now being inoculated by Tunnicliff and White in the Boston Vaccine Laboratory, with a view to produce measles antiserum on a larger scale.

The foregoing review of the literature on experimental inoculation in animals brought me to the general conclusion that, in spite of a large percentage of negative results, measles can be transmitted to nearly all of the experimental animals, the monkeys being the most susceptible; rabbits, guinea-pigs, goats, sheep and horses follow in order of susceptibility. Cats, dogs and mice may also be susceptible, but the present data do not warrant acceptance of the fact as established. Animals' susceptibility was almost totally doubted by Hektoen [72] when he made a statement in 1905 to the effect that these animals are not susceptible to the disease. Even Jamporis,[73] as late as 1912, in reviewing the literature on the subject, remarked: "It is believed that monkeys alone, of the lower animals, are susceptible to measles, but further investigation may prove this to be an error, as the experiments of Goldberger and Anderson were often negative in their monkeys." Sellards,[74] who had experienced negative results in every attempt, assumed a skeptical attitude when he said, "There is certainly, at present, no exact proof of the susceptibility of monkeys to measles . . . No criteria have as yet been established by which experimental measles can be recognized definitely and unmistakably . . . Personally, I am not willing to

72. Hektoen, L.: Experimental Measles, J. Infect. Dis. **2**:238, 1905.

73. Jamporis, M.: Résumé of Infectious Diseases, Am. J. Dis. Child. **3**:406 (June) 1912.

74. Sellards, A. W.: Medicine **3**:99 (May) 1924.

accept as established the various characteristics of the virus of measles as worked out in this way."

The numerous experiments on animals seem to indicate that the inoculation of infected material removed from patients with measles, when injected under proper conditions, can produce a certain train of symptoms which, though uncertain and not always coherent, may be interpreted to mean the presence of infection. These symptoms are six: (1) fever, (2) exanthem, (3) enanthem, including Koplik spots, (4) leukopenia, (5) catarrh of the eyes and nose and (6) evidence of malaise, manifested by anorexia, diarrhea, vomiting and loss of weight. These symptoms, when present after an incubation period of variable length, usually much shorter than the accepted number of days seen in human beings, may be taken to mean a causal relation to the inoculation; if so, it can be called a clinically identical measles. Sufficient experimental data on subinoculation and animal passage of measles virus are still lacking, and when there is more evidence of the recovery of the virus from the animals so used, one may be reasonably certain that there is true reproduction of human measles in animals.

NATURAL IMMUNITY AND CONGENITAL MEASLES

From the earliest times it has been known that all human beings are susceptible to measles, as may easily be seen in occasional pandemics, such as that of the Faroe Islands in 1846, in which an observing Danish physician, Panum,[75] found human susceptibility to be almost 100 per cent. It is further known that the offspring of parents who have had measles possess a transient immunity which is almost absolute for the first two months of postnatal life and relative up to the fifth month; only a few infants retain any immunity to the ninth month, so that measles among sucklings is of rare occurrence. This immunity is conferred to the offspring, not through the breast milk as conceived by Petenyi,[76] but through placental blood during the months of gestation, provided that the mother had the infection not later than about three weeks before delivery. Cases are on record in which the fetus apparently enjoyed immunity from the disease with which the mother was afflicted. Thomas,[77] however, cited his own experience which showed the failure of a mother who had measles in the fifth month of pregnancy, to confer immunity to her child, for this child had a typical

75. Panum, P. L.: Beobachtungen über das Maserncontagium, Virchows Arch. f. path. Anat. **1**:492, 1847.

76. Petenyi, G.: Avitaminosen bei mit Muttermilch ernährten Säuglingen, Monatschr. f. Kinderh. **30**:422 (Aug.) 1925.

77. Thomas, L.: Measles, in Ziemssen: Cyclopedia of Practical Medicine, 1878, vol. 2, p. 51.

case of measles at 9 years of age, at the same time that its brothers and sisters had the condition.

If, however, the mother has the infection during one or two weeks just preceding the time of delivery, the infant may be born either with a well developed rash or without any signs of measles, developing such signs within a few days after birth. The so-called cases of congenital measles are those in which the infant is born with a well developed measles rash, signifying that the labor coincided approximately with the eruptions, and that the infection in the mother took place from ten to fourteen days before the onset of labor. There are numerous cases of congenital measles on record, as cited by Ballantyne,[78] who also gives his own observation of one case in which the mother was exposed to measles just ten days before the onset of premature labor. She gave birth to a fetus only 30 cm. long, which soon died. The fetus was covered with generalized erythema in which Ballantyne noted "numerous dark red or purplish spots, one or two on the face, several on the back of the trunk and neck, and a few well marked ones on the lower limbs especially at the ankles."

Ritossa[79] was able to recover from the liver, spleen, kidneys and bone marrow of a still-born infant an organism that corresponded exactly with the diplococcus described by Caronia. This shows that the infection is definitely transmitted to the fetus from the mother by way of placental circulation, resulting in miscarriage or abortion in many cases, or the new-born infant may exhibit symptoms of measles at birth.

When the mother is exposed to measles within a week or ten days before the onset of labor, the infant may be born normally, and yet the mother and the infant may develop the signs of measles almost simultaneously within a few days after delivery, corresponding to the number of days of incubation and invasion. A case is reported by Debré, Joannon and Mariani,[80] in which the infant, who was born normally during the incubation period of the disease with which the mother was afflicted, developed Koplik spots three days after the appearance of the eruption in the mother. Ronaldson[81] also reported the case of a mother who entered the hospital the day after a normal delivery with a typical attack of measles. The infant was nursed by the mother. Daily examination of the infant did not reveal any pathologic process until the

78. Ballantyne, J. W.: Congenital Measles, with Notes of a Case, Arch. Pediat. **10**:301, 1893.

79. Ritossa, P.: Presence of the Measles Organism in a Still-Born Infant of 8 Months, Pediatria **32**:513 (May 1) 1924.

80. Debré, R.; Joannon, P., and Mariani, J.: Congenital Measles, Nourrisson **13**:249 (July) 1925.

81. Ronaldson, G. W.: Measles at Confinement; with Subsequent Modified Attack in Child, Brit. J. Child. Dis. **23**:192 (July-Sept.) 1926.

fourteenth day, when the temperature rose to 99 F., the buccal mucosa became infected and a few Koplik spots were present. There were slight catarrhal symptoms, occasional cough and sneezing. A coarsely punctate erythema covered the chest and abdomen. The following day the eruption was somewhat blotchy, but could not be described as definitely morbilliform.

The cases of congenital measles as well as measles during the first two weeks of life are of interest from the standpoint of etiology and immunity. They throw a considerable amount of light on the nature of infection and mode of transmission as well as on the mechanism of natural immunity.

PASSIVE IMMUNIZATION

The most interesting and valuable contribution of modern research on measles is undoubtedly the discovery of a method of prophylaxis by means of measles convalescent serum. The fundamental principle of this procedure is, of course, a production of passive immunity with the antibodies formed in the blood of the patients who have recovered from the disease, a fact well established in diphtheria and tetanus and anticipated in poliomyelitis and epidemic parotitis.

The idea thus is by no means a new one, for in 1896, Weisbecker [82] in Germany published his detailed account of the use of measles convalescent serum for therapeutic purposes, while Leydens, Huber and Blumenthal [83] treated nine patients with measles with the serum in the following year.

Cenci,[84] however, was the first to use the convalescent serum for purposes of passive immunization as early as 1901 and again in 1906, the experiences with which were published in 1907. He prepared the serum from a child who was one of the first to have the disease and injected this serum into three brothers in one family and one child in another. The first three had two other brothers, aged 2 and 9 years, respectively, in whom he did not make any injections. The fourth child had three brothers who had not had measles and to whom injections were not given. For a month after the injections, all these children were repeatedly exposed to measles but were completely protected. The two brothers of the first three children had measles. The epidemic lasted for two months after the injections were made, but none of the four children who had received injections contracted the disease. In 1906,

82. Weisbecker: Heilserum gegen Masern, Ztschr. f. klin. Med. **30**:312, 1896.

83. Leydens, Huber, and Blumenthal: Berl. klin. Wchnschr. **1897**:; cited by M. v. Gruber, in the introductory remarks in Degkwitz: Die Masernprophylaze und Ihre Technik, Berlin, Julius Springer, 1923, p. 6.

84. Cenci, F.: Alcune esperienze di sieroimmunizzazione e sieroterapia nel morbillo, Riv. di clin. pediat. **5**:1017, 1907.

there was another epidemic in the same community, which proved to be much more severe, in which three of the four children who had been immunized in the 1901 epidemic had measles, indicating that the passive immunity conferred by convalescent serum is of short duration.

Nicolle and Conseil, two French physicians practicing in Tunis, in 1918, published their account of successful prophylaxis of measles with convalescent serum in 1916, which apparently inspired Richardson and Connor in the United States to attempt passive immunization in fourteen persons with complete success. About this time, there appeared in Germany one of the most energetic workers in serum treatment of persons with measles. Working at first in Pfaundler's clinic in Munich, Degkwitz [85] published, in 1920, his first article in which he reported successful inoculation for passive immunization in over 700 cases, and during the following three years, he claimed to have immunized more than 5,000 children by his method. Following his suggestions, many workers in this field have since added rather rapidly to the statistics of serum prophylaxis; among these are: Pfaundler in Munich; Kutter, Müller and Glaser in Berlin; Manchot and Reiche, and Kleinschmidt in Hamburg; Zschau in Nurenberg; Rietschel in Wurtenberg; Goebel in Jena; Schilling in Chemnitz; Zimmermann in Greifswald; Pilz in Magdeburg; Feer in Zurich; Krves in Amsterdam; von Torday in Budapest; Jervell in Stockholm; Torres and Pacheco in Brazil, and many others too numerous to mention. All have followed the logic of Degkwitz and have brought the total of successful inoculations with measles convalescent serum well above 1,000 in about two years.

When recent convalescent serum is not available, as is often the experience during an epidemic, Degkwitz and others recommend the use of the serum of adults with a history positive for measles, providing the dosage be large, usually 30 cc. or more, although the results are not uniformly certain. Von Torday [86] reported 116 injections of adult serum with failure to obtain protection in only twelve cases. Rietschel [87] recommended the injection of from 20 to 25 cc. of blood from the mother or relatives who have had measles. Jervell [88] inoculated two

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85. Degkwitz, R.: Ueber Versuche mit Masernrekonvaleszentenserum, Ztschr. f. Kinderh. **25**:134, 1920; **27**:171, 1920). His subsequent publications on convalescent serum are as follows: Zur individuellen Masernprophylaxe, München. med. Wchnschr. **67**:649, 1920; Züchtung des Masernerregers und Masernschutzimpfungen mit lebenden Erregern, Monatschr. f. Kinderh. **22**:186, 1921-1922; Ueber Masernschutzserum, Deutsche med. Wchnschr. **48**:26, 1922; Die Masernprophylaxe und Ihre Technik, Berlin, Julius Springer, 1923.

86. Von Torday, F.: Jahrb. f. Kinderh. **102**:213, 1923.

87. Rietschel, H.: Zur Frage der prophylaktischen Injektion von Normal Serum als Masernschutz, Deutsche med. Wchnschr. **49**:1386, 1923.

88. Jervell, O.: Norsk. Mag. f. Laeger **83**:601, 1922.

children under 2 years and from 20 to 25 cc. for older ones. Hilsinger [93] injected 20 cc. of adult blood into 100 persons either directly into the muscle or after adding 10 per cent of a 3 per cent sodium citrate solution. The results were inadequate, although the course of the disease when developed was mild. He suggested that the effect of inoculation may be due to nonspecific agents in the serum. Goebel [94] observed that inoculation with adult blood caused only one failure in the twenty-two cases in which he tried it. Kovacs [95] obtained protections in thirty-five of forty persons whom he inoculated according to Rietschel's method. Bivings [96] used 15 cc. of clear serum obtained by letting 35 cc. of whole blood from a parent stand in a cool place, and produced partial protection.

The method advised by Degkwitz is the sterile collection of blood from seven to nine days after defervescence. Serums are mixed and kept on ice with 1 drop of 5 per cent phenol added to every 40 cc. of mixture. He established a system of dosage by estimating what is known as "unit dose," which is from 2.5 to 3 cc. of mixed serum given befor the fourth day of incubation, which is sufficient to protect a child up to the age of 14 years. If serum from a single donor is used, at least from 4 to 7 cc. must be given. Injections made on the fifth or sixth day require 2 units for protection, while on the seventh day results are uncertain, and on the eighth day or thereafter they have no effect. If a smaller dose is given early, a benign form of measles results, with subsequent active immunization. According to his conception, the antibody formation reaches its maximum on the seventh day after convalescence is established, but its concentration falls rapidly, and hence the blood should be withdrawn when this maximum is reached.

Some authors recommend that serum be inactivated. Jordan,[97] for example, gave the following method:

> Blood is withdrawn under aseptic conditions much the same as for a Wassermann test. According to the age of the patient, we remove from 30 cc. to 500 cc. of blood, allow it to coagulate in the refrigerator for several hours, and decant the serum. This is now being placed in vials containing five or six cubic centimeters. It is inactivated at 56 C. for thirty minutes and if kept more than a week is again inactivated for the same period before use. Some serum has been

93. Hilsinger, W.: Erwachsenenblut-Einspritzungen zum Masernschutz, Arch. f. Kinderh. **76**:211, 1925.

94. Goebel, F.: Erfahrungen mit der Degkwitzschen Masernprophylaxe, Ztschr. f. Aerzt. Fortbild. **21**:358, 1924.

95. Kovacs, E.: Erfahrungen mit der Rietschelschen Masernprophylaxe, Deutsche med. Wchnschr. **51**:1703, 1925.

96. Bivings, L.: Measles Prophylaxis by Use of Parent's Blood Serum, South. M. J. **20**:735 (Sept.) 1927.

97. Jordan, H. P. B.: Measles Immunization, Rhode Island M. J. **9**:71 (May) 1926.

TABLE 4.—*Chronological List of Prophylactic Inoculations*

Author and Source	Amount and Time of Injection*	Total Number	Complete Protection	Incomplete or No Protection
Nicolle, C., and Conseil, E.: Bull. et mém. Soc. méd. d. hôp. de Paris **42**: 336, 1918	4 cc. c.s. repeatedly on 7th day of exposure	2	2	0
Richardson, D. L., and Connor, H.: J. A. M. A. **72**: 1046 (April 12) 1919	7 to 25 cc. c.s. with nasal swabs	18	16	2
Degkwitz, R.: Ztschr. f. Kinderh. **25**: 134, 1920	2.5 to 3 cc. c.s. before 4th day of incubation	700	Successful	
Glaser, F., and Müller, H.: Med. Klin. **17**: 649, 1921	3 to 6 cc. c.s.	7	7	0
Torres, M., and Pacheco, G.: Arch. latino-am. de pediat. **14**: 305, 1920	.....	5	3	2
Von Torday, F.: Ztschr. f. Kinderh. **29**: 148, 1921	2 to 6 days of incubation (Degkwitz dose)	261	246	15
Zschau: München. med. Wchnschr. **68**: 1049 (Aug.) 1921	Average 10 cc. and 3 cc. on 4th to 10th day of incubation	39	37	2
Manchot, G., and Reiche, F.: Med. Klin. **17**: 1230 (Oct. 9) 1921	3 to 5 cc. c.s.	155	139	11
Kutter, P.: Ztschr. f. Kinderh. **30**: 90 (Aug.) 1921	Degkwitz method	145	141	4
Ibid. **36**: 119, 1923	4 cc. pooled c.s.	255	127	28
Maggiore, S.: Pediatria **29**: 873, 1921	2 cc. and 4 cc. repeated after 48 hours	Several hundred		
Kohler, O.: Der prakt. Aerzt. **19**: 282, 1922	Degkwitz dosage 4th or 5th day of incubation	29	27	2
McNeal, M. D.: J. A. M. A. **78**: 340 (Feb. 4) 1922	6 cc. c.s.	16	12	4
Nobécourt, P., and Paraf, J.: Presse méd. **30**: 497 (June 10) 1922	3 cc. c.s. before 6th of incubation	20	20	0
Ibid. **37**: 449, 1923	3 cc. of heated and unheated c.s.	14	14	0
Zimmermann, L.: Deutsche med. Wchnschr. **48**: 1701 (Dec. 22) 1922	Degkwitz method, 7th to 17th day of incubation	19	15	4
Blackfan, K. D., and Peterson, M. F.: Ohio State M. J. **19**: 97 (Feb.) 1923	5 cc. c.s. 2 to 5 days after exposure	59	54	5
Salomon, G.: Deutsche med. Wchnschr. **49**: 1151, 1923	.....	62	37	25
DeLong, S. J. T., and Bernard, E.: Bull. et mém. Soc. méd. d. hôp. de Paris **47**: 500 (March 23) 1923	5th to 8th day of incubation	16	15	1
Von Torday, F.: Jahrb. f. Kinderh. **102**: 213, 1923	20 cc. of whole blood (convalescent)	116	104	12
Kundratitz, K.: Wien. med. Wchnschr. **73**: 1200, 1923	1 to 2 cc. c.s.	39	A few failures	
DeStefano, S.: Pediatria **31**: 781, 1923	5 cc. whole blood at appearance of palpebral edema	7	0	7
Davis, R. C.: M. Clin. N. Amer. **7**: 1259 (Jan.) 1924	5 cc. on 1st day, 10 cc. on 2d day	52	50	2
Weaver, G. H., and Crooks, T. T.: J. A. M. A. **82**: 204 (Jan. 19) 1924	5 cc. of c.s. during first week	63	44	1
Zingher, A.: J. A. M. A. **82**: 1186 (April 12) 1924	2.5 to 7.5 cc. serum or plasma 1 to 8 days of incubation	102	92	10
Pesetke, S. E.: Am. J. Dis. Child. **28**: 122 (July) 1924	2 to 4 cc. c.s. in first 4 days	50	46	4
Sinclair, C. G., and Avery, S. D.: Military Surg. **55**: 697 (Dec.) 1924	4 to 10 cc.	80	77	3
Prochazka, J.: Cas. lék. cesk. **64**: 100, 1925	2.5 cc. c.s.	90	85	5
Debré, R., Bonnet, H., and Decam, J. C.: Rev. d'Hyg., January, 1926	.....	...	83.5%	12.5%
Lenstrup, E.: Ugesk. f. Laeger. **88**: 218 (March 4) 1926	Late in incubation	17	12	5

* In this table c.s. indicates convalescent serum.

TABLE 4.—*Chronological List of Prophylactic Inoculations—Continued*

Author and Source	Amount and Time of Injection*	Total Number	Complete Protection	Incomplete or No Protection
Anderson, M. S., and Wulff, F.: Ugesk. f. Laeger. **88**: 216, 1926	5 to 15 cc. c.s.	91	86	5
Townsend, J. H.: Boston M. & S. J. **194**: 809 (May 13) 1926	9 cc. whole convalescent blood	63	0	63
Toomey, J. A.: Am. J. Dis. Child. **32**: 402 (Sept.) 1926	2.5 to 5 cc. c.s. first 8 days of exposure	368	347	21
Park, W., and Freeman, R. G.: J. A. M. A. **87**: 556 (Aug. 21) 1926	3 to 10 cc. plasma during first 5 days of exposure	979	136	253
Haas, S., and Blum, J.: J. A. M. A. **87**: 558 (Aug. 21) 1926	5 to 10 cc. plasma or whole blood before 7th day	269	182	87
Freeman, R. G., and Freeman, R. G. Jr.: Arch. Pediat. **43**: 563, 1926	1 to 3 days	22	6	16
Ogawa, G.: J. Pediat. Tokyo, 1926, no. 303, p. 1214	3 to 10 cc. c.s. 3 to 10 cc. normal blood	4 10	3 6	1 4
Aoyama, T.: J. Pediat. Tokyo, 1926, no. 303, p. 1224	20 to 30 cc c.s.	6	6	0
Kingsbury, A. N.: Lancet **1**: 7 (Jan. 1) 1927	2 to 3.5 cc. c.s.	395	367	28
Karelitz, S., and Levin, S.: Am. J. Dis. Child. **33**: 408 (March) 1927	5 cc. c.s., 25 cc. adult serum, 75 cc. adult whole blood	77	66	11
Baron, C.: Med. Klin. **23**: 48, 1927	9 to 11 days	No protection, no attenuation		
Benson, W. T., and Lawrie, J. D. H.: Edinburgh M. J. **34**: 216 (April) 1927	5 cc. plasma before 4th day	12	11	1
Richardson, D. L., and Jordan, H. P. B.: Am. J. Pub. Health **17**: 607 (June) 1927	6 cc. c.s.	186 19 550	99 .. 418	 19 132
Shizume, S.: J. Pediat. Tokyo, no. 300 and 303	20 to 30 cc. adult whole blood	10	8	2
Jordan, H. P. B.: Rhode Island M. J. **7**: 71, 1926	5 to 12 cc. c.s., 3 to 11 days 6 to 18 cc. c.s., 5 to 10 days	24 72	23 69	1 3
Macnamara: M. J. Australia **2**: 50, 1926	25 cc. citrated whole blood, on 5th day	1	1	
Emmanuele, A.: Pediatria **34**: 30, 1926	Caronia's vaccine	45	41	4

* In this table c.s. indicates convalescent serum.

children with 10 cc. of adult blood. Salomon [89] used normal serum (10 to 15 cc.) for prophylactic purposes in seventy-six infants, but only forty were protected. Kutter [90] used adult serum in fifteen children (6 to 15 cc.) on the fourth day of incubation, with only one failure. Gerlach [91] used it with success in doses of from 20 to 30 cc., taking the entire defibrinated mass. Debré and his co-workers [92] were successful in using adult blood, the dose being from 12 to 15 cc. for

89. Salomon, G.: Die prophylaktische Injektion von normal Serum als Masernschutz, Deutsche med. Wchnschr. **49**:1151, 1923.

90. Kutter, P.: Ztschr. f. Kinderh. **36**:119, 1923.

91. Gerlach, H.: Ueber prophylaktische Schutzsimpfung mit defibriertem Erwachsenenblut bei Masern, Monatschr. f. Kinderh. **28**:236, 1924.

92. Debré, R.; Joannon, P.; Bonnet, H., and Cros-Decam, J.: Emploi du sang et du sérum d'adulte ayant eu la rougeole autrefois, pour la prévention de cette maladie, Bull. et mém. Soc. méd. d hôp de Paris **49**:682 (May 14) 1925.

kept over a year with the addition of .75 per cent tricresol for a preservative, seeming to hold its potency during this period.

Other materials used for prophylactic purposes for measles are recommended from time to time. Zingher [98] recommended the use of whole blood or plasma only in double the dosage required of serum. He used from 1 to 2 cc. of 5 per cent sodium citrate when drawing the blood and injected it intramuscularly. In New York, the plasma, under his recommendation, was put up in 3 and 6 cc. vials and in 30 cc. bottles, for general distribution. De Castro [99] put the dried serum in ampules which kept indefinitely. Schilling [100] used from 0.2 to 0.5 cc. of blister fluid, obtained by means of cantharides, in fourteen cases and only one patient was protected, while Modinos [101] used from 3 to 5 cc. of similar fluid and was apparently successful. In 1922, Galli [102] reported the use of diphtheria antitoxin and of normal horse serum in children in an asylum, and 50 per cent were protected. Of those who had been given normal horse serum during the incubation period, all but three were protected. In 1906, Cenci recorded the shortening of a measles epidemic by giving diphtheria antitoxin. Pontano and Alba [103] gave from 5 to 10 cc. of normal horse serum to forty-two children and only three of them developed attenuated measles; he concluded that the serum was as efficient as convalescent serum. Seven other patients were successfully inoculated with diphtheria antitoxin due to the beneficial action of the horse serum.

Table 4 which gives a statistical summary as to the number of immunizations actually reported in the literature reveals that not less than 10,000 persons have thus far been immunized with measles convalescent serum in doses varying from 2.5 to 10 cc. A small number of persons received adult blood which was thought to contain measles antibodies due to previous illness. Of this total, approximately 9,000 persons have been successfully protected on one or more exposures. The remaining 1,000 failures were probably due to either inadequate doses of serum or delayed inoculations. The majority of persons in whom the inoculation was not successful, however, had measles in greatly modified or attenuated form, although there were persons

98. Zingher, A.: Convalescent Whole Blood, Plasma, and Serum in Prophylaxis of Measles, J. A. M. A. **82**:1180 (April 12) 1924.

99. De Castro, J. E.: Arch. españ. de pediat. **6**:517 (Sept.) 1922.

100. Schilling, E.: Zur Masernprophylaxe, Klin. Wchnschr. **1**:2471 (Dec. 9) 1922.

101. Modinos, P.: Bull. et mém. Soc. méd. d. hôp. de Paris **50**:404 (March 12) 1926.

102. Galli: Immunizzazione contra il morbillo, Pediatria **30**:898 (Oct.) 1922; abstr. in J. A. M. A. **79**:1885 (Nov. 25) 1922.

103. Pontano, T., and Alba, C.: Ann. d'ig. **37**:515 (Aug.) 1927.

properly inoculated who presented typical attacks of measles. Therefore, in attempting passive immunization of those who have come in contact with patients who had measles, it is of utmost importance to note the following points:

1. Recent convalescent serum is most effective if withdrawn from seven to nine days after defervescence.

2. Mixed serum is far superior to serum from a single donor.

3. The optimum dosage for average children under 12 years of age seems to be from 3 to 6 cc. of serum.

4. The most desirable time for inoculation seems to be about the fourth day of incubation or a little earlier, as too early or too late administration brings about an uncertain result.

The duration of passive immunity conferred by this method may be estimated only with approximation, for experimentation along this line is extremely difficult and often impossible. Von Torday saw absolute protection lasting for seventy-two to seventy-five days after serum was given in three cases, while McNeal and Weaver and Crooks believed two months to be the limit of immunity. The concensus of opinion of reliable observers seems to indicate that the duration varies from two to six months. In cases in which protection seems effective on repeated exposures covering a period of two or three years, an element of active immunization may be thought to be present.[104]

ACTIVE IMMUNIZATION

On account of the short duration of passive immunity conferred by an injection of convalescent serum, a method of inducing a more permanent immunity must be sought. The process of active immunization is often designated as "morbillization" (rougeolation of French writers), a term corresponding to "variolization" in smallpox. The term "sero-attenuation" has also come to be used to designate this procedure.

The first attempt along this line was made by Herrman[105] of New York, who, in 1915, endeavored to induce a mild form of the disease in young infants. Utilizing the relative immunity in infants under 5 months of age, he inoculated forty such infants by gently rubbing the nasal mucosa with nasal washings collected from patients with measles, twenty-four hours before the eruption appeared. Some of these inoculated infants showed a rise of temperature between the eighth and fourteenth day, and in a few cases some indistinct spots were noted on the face and body between the fourteenth and eighteenth day. Four

104. Lyon, G. M.: The Duration of Passive Immunity in Measles Prophylaxis, W. Virginia M. J. **22**:291 (June) 1926.

105. Herrman, C.: Immunization Against Measles, Arch. Pediat. **32**:503, 1915.

years later, Herrman [106] testified that only two of these had since contracted typical measles. He expressed the opinion that the duration of immunity produced in this way lasts at least two years.

In 1921, two Japanese workers, Hiraishi and Okomato [107] attempted active immunization by small repeated doses of infected blood. They used whole blood withdrawn from patients with measles during the early stages of the disease and diluted to 100, 1,000 and 10,000 with 1 per cent citrated saline, which was given subcutaneously in quantities of from 0.5 to 1 cc. of the 1 : 10,000 dilution for the initial injection, followed in three weeks with second inoculation of the same amount, using the 1 : 1000 dilution. They gave these injections to forty-four children ranging in age from 1 to 10 years. Unfortunately, their results are not uniform and clearcut, but they indicate at least that the injection of infected blood in the minimum doses is attended by some degree of immunity so as to resist the reinoculation with the injection of a greater quantity.

In 1921, at a Pediatric Congress in Jena, Degkwitz [108] read a paper in which he stated that the injection of the culture of conjunctival and pharyngeal secretions on proper mediums containing human albuminous fluid in the susceptible children induced from twelve to fifteen days afterward nasal catarrh and a slight rise of temperature. Several months after the inoculation, these children still proved to be refractory to measles on repeated exposures.

In 1923, Nicolle and Conseil [109] used a "sero-vaccination" method which consists in successive inoculations of 10 cc. of convalescent serum followed fourteen hours later with 1 cc. of blood from patients with measles. This method far exceeds that of passive immunization in the duration of the immunity obtained.

In 1923, Savini [110] used attenuated virus for active immunization. He took equal amounts of 5 per cent citrate and blood, heated the mixture for fifteen minutes at 56 C. or added 1 per cent phenol, making the phenol content 0.5 per cent of the total mixture. He injected subcutaneously from 4 to 5 cc. of this mixture morning and evening on three successive days (from 1 to 2 cc. being sufficient for young infants). The injection was not attended by any reaction, and the induced

106. Herrman, C., in discussion on Blake and Trask: Experimental Measles, J. A. M. A. **77**:192 (July 16) 1921.

107. Hiraishi, S., and Okamoto, K.: Prophylactic Inoculation Against Measles, Japan Med. World, Tokyo **1**:10, 1921.

108. Degkwitz, R.: 33 Tag. d. Deutsche. Gesell. f. Kinderh., May 12-14, 1921, Monatschr. f. Kinderh. **22**:186, 1921.

109. Nicolle, C., and Conseil, E.: Acquisitions nouvelles sur la rougeole (Vaccination prevéntive. Conditions de la contagion), Compt. rend. Acad. d. sc. **171**: 160, 1923.

110. Savini, E.: Essai de vaccinothérapie prevéntive dans le typhus exanthematique, la scarlatine, et la rougeole, Compt. rend. Soc. de biol. **89**:694, 1923.

immunity was lasting, although his observations are limited to only seven cases.

In 1926, Zingher [98] advocated a combination of passive and active immunization. This method follows Herrman's method of nasal swab in children older than 5 months of age, and from twenty-four to forty-eight hours after the swabbing, convalescent serum is given in appropriate amounts. This procedure induces a mild attack of measles, which gives a lasting immunity. The same idea is followed by Forbes and Green [111] of Denver, who produced modified measles in seven children by giving blood and serum in small amounts and not too early in the incubation period.

The most recent attempt at active immunization is that of Debré, Joannon and Papp,[112] who, by using the diluted blood containing measles virus, endeavored to produce immunity without inducing an attack of even a mild form of the disease. In children, aged from 2 to 4 years, 1:400 cc. of blood diluted in saline given subcutaneously caused a moderately high temperature, with stomatitis, catarrh and a slight eruption in from seven to ten days; but 1:800 cc. of the same dilution produced only a transient leukopenia, which reached its minimum in from eight to ten days. After three weeks, inoculation was repeated with 1:400 cc. The immunity conferred by this method may be enduring, but definite data are still lacking.

In reviewing the foregoing attempts at active immunization from the standpoint of a clinician, it becomes self-evident that the best method is necessarily the one which is most practicable. Any method which induces an attack of the disease, even though it is mild and benign, is not worthy of wide application, nor is any naive procedure commendable, such as rubbing of the mucosa with a nasal swab from patients with measles. In order to be practical, the method should be scientific and be at the command of the practitioner whenever needed. This means that the vaccine virus must be preserved with a fairly constant degree of potency, and its immunologic titer must be ascertained with approximate accuracy. That procedure which produces no visible reaction and yet induces reasonably lasting immunity must be sought.

ATTENUATION OR MODIFICATION OF MEASLES

Frequent mention is made of "attenuation" or "modification" of measles in connection with various problems of passive and active immunization, terms which need a little further elucidation. The attenuated or modified measles must be distinguished from a benign form of typical measles and also from a so-called abortive type of the

111. Forbes, R. P., and Green, B.: Modified Measles, J. A. M. A. **89**:1601 (Nov. 5) 1927.

112. Debré, R.; Joannon, P., and Papp, K.: L'immunization active contre la rougeole, Ann. de méd. **20**:343 (Oct.) 1926.

disease. It may be regarded as a new form of measles induced by injection into susceptible persons of morbid doses of infected blood or other materials containing the contagium of the disease. It can be induced also by injecting convalescent serum either in insufficient quantities or at inopportune times. Zingher produced modified measles by first swabbing the mucosa with nasal secretions and later by injecting the proper amount of convalescent serum, as already referred to. Regan [113] produced this form of the disease in fifteen cases by administering convalescent serum late in the incubation period (between the sixth and ninth day) in doses of from 8 to 10 cc. which, he thinks, is far more logical than an induction of simple passive immunity. Following this suggestion, Forbes, Green and Mugrave [114] saw a high percentage of modified measles in fifty-five cases in which convalescent serum was used, and later Forbes and Green [115] saw six of seven persons who had received blood from a "family donor" develop modified measles. To produce modified measles, they recommended that serum or blood be given in not too large amounts and not too early in the incubation period. Injections given between the fifth and the eighth day after exposure have been found effective for this purpose.

It is of interest to note some outstanding differences in the symptomatology of modified measles as compared with that of ordinary measles. The following are the outstanding points of distinction: [116]

1. The incubation period is much more prolonged, ranging from eighteen to twenty-four days, and there is usually no rise in temperature.

2. The period of invasion is short, since the coryza may be mild or entirely lacking, often amounting to a mild degree of snuffles.

3. The prodromal signs are altered, and the enanthem and Koplik spots are either atypical or absent, but the so-called prodromal rashes are more common than in typical measles.

4. The exanthem is less pronounced, sometimes discrete, amounting to a few localized macules usually appearing on the body, the face and neck generally being free from eruptions. Sometimes the rash may become ecchymotic as it fades.

5. The constitutional symptoms are less marked, as evidenced by a lower temperature; usually there is no fever, or the temperature may be from 100 to 101 F.

113. Regan, J. C.: The Symptomatology of Measles Modified by Late Serum Administration, J. A. M. A. **83**:1763 (Nov. 29) 1924.

114. Forbes, R. P.; Green, B., and Mugrave, E. R.: Modified Measles in Private Practice, Colorado Med. **27**:222 (July) 1927.

115. Forbes, R. P., and Green, B.: Modified Measles, J. A. M. A. **89**:1601 (Nov. 5) 1927.

116. Debré, R., and Ravina, with the collaboration of Bonnet and Benoist: La rougeole modifiée par l'injection prévéntive de serum de convalescent, Bull. Soc. méd. d. hôp. de Paris **47**:226 (Feb. 9) 1923.

6. Complications are practically unheard of.

7. Immunologic reactions are characteristic. In tuberculous children, the Pirquet test remains positive throughout the course of a modified measles, whereas during a typical attack of ordinary measles, it usually is negative.

THERAPEUTIC USE OF CONVALESCENT SERUM

The gravity of some cases of measles often calls for the administration of convalescent serum for therapeutic purposes, and if the antibody content of such serum is sufficient as in diphtheria antitoxin as it is used today, its use for the amelioration of symptoms and complications is rational. The first to use this therapeusis was Weisbecker,[117] who, in 1896, reported four cases of measles complicated with pneumonia in which the patients were treated by administration of from 10 to 18 Gm. of convalescent serum, and in all four cases, the injections were followed by satisfactory recovery.

During an extensive epidemic of measles in Ancona, Italy, in 1914, Majoli[118] injected from 15 to 50 cc. of convalescent serum on the second or third day of the onset of fever in eight cases, and observed that the febrile course was much shortened or the fever fell immediately after the injection and that the exanthem was greatly alleviated in degree and in duration, and was followed by practically no desquamation. On the whole, his patients who were treated with serum showed a much milder form of the disease and consequent low mortality than the untreated patients.

In 1918, Ribadeau-Dumas and Brissaud[119] treated an Arab for an extremely malignant form of measles by giving an infusion of 100 cc. of citrated blood taken on the eighth day from a person convalescing from measles. This proved to be beneficial. This patient had been seen to suffer from hyperpyrexia, ecchymotic eruption, epistaxis, albuminuria, "ataxo-adynamic" phenomenon, almost on the verge of collapse, but within several hours after the injection he showed a drop in temperature and general improvement in his condition.

Terrien[120] treated an infant, aged 13 months, for malignant measles; the rash faded suddenly, the temperature climbed to 41 C. (104 F.), and coma lasted for several days. On the fifteenth day, 20 cc. of citrated blood from a brother who had had measles six months previously was given. Three days later, the child began to show evidences of recovery.

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117. Weisbecker: Ztschr. f. klin. Med. **30**:312, 1896.

118. Majoli, U.: La cura del morbillo col siero di morbillosi convalescenti, Policlinic **22**:1229 (Sept. 12) 1915.

119. Ribadeau-Dumas, L., and Brissaud, E.: Un cas de rougeole grave traitee per la transfusion du sang citrate d'un rougeoleux gueri, Bull. et mém. Soc. méd. d. hôp. de Paris **42**:110 (Feb.) 1918.

120. Terrien, E.: Rougeole maligne et plasmothérapie, Bull. et mém. Soc. méd. d. hôp. de Paris **63**:1134, 1919.

In 1922, Maniel [121] of Constantinople treated a soldier who had measles and pneumonia, and 20 cc. of blood withdrawn on the fifteenth day of convalescence proved effective in bringing about his recovery.

Cogné [122] reported a case of congenital measles in an infant born while the mother had the disease in the full eruptive stage. As far as he is aware, this is the first instance in which the therapeutic measure has been applied to the newly born. When 2 days old, the infant received 3 cc. of convalescent serum, and was kept on the breast of the mother who was suffering from active measles. The baby had a slight fever on the following day, and four days afterward had a morbilliform rash over the body and thighs, which, however, faded away within two days. Catarrh was not noted at any time.

In 1924, Weaver and Crooks [123] gave from 35 to 40 cc. of convalescent serum to each of two patients on the day the rash appeared. The serum had no effect on the course of the disease in either case, although the authors add that "their failure need not be attributed to absolute lack of value in the serum treatment of measles."

In the 1926 epidemic of measles which occurred at Berea College, Ky., Cowley [124] had an opportunity to give from 3 to 5 cc. of convalescent serum to 156 students just as soon as the Koplik spots appeared. Comparing the course of the disease in the epidemic with a similar outbreak two years previously, Cowley cited a significant observation in the following manner:

TABLE 5.—*Comparison of Facts in Two Measles Epidemics*

	1924	1926
Average temperature on day of admission to the hospital.....	102.2 F.	102.3 F.
Average of the highest temperature reached by each case.....	103.9 F.	102.3 F.
Average number of days in the hospital with rising temperature..	5.64	3.2
Average number of days in the hospital.....	10.12	5.64
Number of patients with temperature above 104 after first day....	43	11
Percentage of patients whose temperature increased after first day	73	44.5

The author noted a singular absence of complications during the 1926 epidemic as compared with previous ones, which, he believed, was due to the effect of immune serum.[125] Some of the cases which are

121. Maniel, M.: De la transfusion sous-cutanée dans un cas de rougeole grave, Soc. de méd. française, seance du 20 Juillet, 1922, p. 222, cited by Cheinisse, L.: Les essais d'hermatothérapie prevéntive et curative dans la rougeole, Presse méd. **30**:846 (Sept. 30) 1922.

122. Cogné, R.: Use of Convalescent Serum in a Case of Congenital Measles, Internat. Clin. **1**:99 (March) 1924.

123. Weaver, G. H., and Crooks, T. T.: The Use of Convalescent Serum in the Prophylaxis of Measles, J. A. M. A. **82**:204 (Jan. 19) 1924.

124. Cowley, R. H.: The Treatment of Measles by Immune Serum, Therap. Gaz. **50**:387 (June) 1926.

125. Cowley, R. H.: Problem of Measles; Possible Solution, Kentucky M. J. **24**:365 (Aug.) 1926.

quoted by the author, however, seem so miraculous that a shadow of doubt is cast as to his accuracy in observation. For example, a case of measles is cited in a weak person convalescing from unresolved pneumonia and discharging ears. A single injection of 6 cc. of convalescent serum is said to have caused the rash to fade on the following day and the temperature to become normal; after several days, however, the temperature again climbed to 103.8 F., the ears again began to run and the tenderness about the mastoid was so great as to prohibit touching the part. Another injection of 10 cc. of the serum again brought about a complete transformation in the condition on the following day!

Aside from the use of convalescent serum, the Italian investigators claim to have brought out an effective vaccine for the treatment of patients with measles. Sindoni [126] made her vaccine by disintegrating cultures of the micro-organism of measles obtained by a process of biologic lysis with the serum of convalescents by the classic method of Di Cristina and Caronia. She applied this vaccine therapeutically in eighteen cases of measles at the beginning of the eruption, and the patients were benefited by its use. These cases show that the duration of the disease was decreased and the individual symptoms were rapidly improved. All the patients recovered, and there was an almost entire absence of complications. Although her experiences are limited to these eighteen cases, and therefore permit no definite conclusions, she is of the opinion that treatment with vaccines obtained by lysis is absolutely harmless, and that great benefit will be derived from its early and rational use.

Treatment with vaccines in any acute infectious disease is at most undependable, for the underlying principle of any vaccine therapy is production of active immunization, which usually requires a reasonably long time for the development of immune bodies in response to the antigens contained in the vaccine. In an acute febrile disease with a fairly definite course like measles, therefore, it becomes exceedingly problematic whether an attempt to induce active immunity by means of vaccines is consistent with rational therapeusis. In the presence of distressing symptoms in cases of malignant measles, especially in the presence of threatening complications, a measure which is far more desirable is to administer immune bodies in sufficient quantities at the earliest possible moment, with the view to alter the course of the disease at once for the better.

IMMUNOBIOLOGY OF MEASLES

There are certain other immunologic observations that throw considerable light on the character of measles as a specific infectious dis-

126. Sindoni, M. B.: Vaccine Treatment of Measles, Pediatria **33**:173, 1925.

ease. Blake and Trask,[127] in a preliminary paper published in 1921, related an observation to the effect that a measles virus attenuated by animal passage, if injected intracutaneously in small amounts, will produce a local reaction without evidence of a subsequent general infection. This local reaction is characterized by a cutaneous edema of from twenty-four to forty-eight hours' duration, followed in some cases by a local exanthem limited to the skin immediately adjacent to the site of injection. This is practically a specific skin test, analogous to the Schick and Dick tests, and has since been confirmed by Tunnicliff with the filtrate of her diplococcus and also by DeVilla with that of Caronia's organism, to which reference has already been made.

Another interesting observation comes from Debré and his associates [128] at the Children's Hospital of Paris. When they injected subcutaneously from 1 to 5 cc. of human convalescent serum, taken from seven to nine days after defervescence, into a patient with measles at the beginning of the period of invasion just as the catarrhal symptoms and Koplik spots appeared, but before the beginning of any eruptions, they found that when the rash appeared there was a phenomenon of inhibition about the point of injection varying in size with the amount of serum injected. It is usually about the size of a 5 franc coin, but may be as large as the palm of the hand. Normal human or goat serum failed to produce any such phenomenon. This is a constant reaction obtained only with the serum containing what the French investigators call "immunisines." Injection after the appearance of the rash has no effect, and hence differs from the blanching test of Schultz-Carlton in scarlet fever. The test was later repeated and its validity confirmed by Keller and Moro.

These observations, together with the numerous facts of immunity already reviewed, form the foundation of a brilliant hypothesis as to the nature and mechanism of measles eruption advanced by Pirquet in a special monograph. According to this author, measles is called a "specific reactive disease," by which is meant a disease in which the human organism becomes ill by the action of its specific products on the pathogenic substance. This is supported by the fact that measles has a fairly definite and constant incubation stage, during which the system is busily engaged in the production of specific antibodies with which it battles against the infecting microbes. Pirquet assumes that the specific antibodies in measles are two in kind, namely, the lysins and the antitoxins. Lysins, as is well known, dissolve the bacterial mem-

127. Blake, F. G., and Trask, J. D.: Experimental Measles, J. A. M. A. **77**:193 (July 16) 1921.

128. Debré, R., Bonnet, H., and Broca, R.: Sur l'inhibition locale de l'eruption morbilleuse par l'injection préalable de serum de convalescent, Compt. rend. Soc. de biol. **89**:70 (June) 1923.

brane and antitoxins neutralize their toxins. According to his assumption, the measles rash is merely a result of the action of lysins which are the first to be formed soon after the infection, which reaches its maximum when the rash appears. With the fading of the eruption, another kind of antibody, the antitoxin, is formed under the stimulus of the toxins which were liberated by the action of the lysins, reaching its maximum from seven to nine days after defervescence. On this point, Keller and Moro [129] remark as follows:

> If there is only a lytic antibody in the serum, then it ought to be possible at some time when there are micro-organisms in the skin to cause an outbreak of measles spots by applying convalescent serum to the skin. But if there are two antibodies, a lytic and an antitoxic one, just the opposite would occur—the toxic inflammation, the exanthem, caused by the toxins of the dissolved micro-organisms, would be prevented and there would be a gap in the exanthem at the point where the serum was applied.

The latter phenomenon is exactly what has happened according to the experiments of Keller and Moro, as well as those of Debré and others.

ANIMAL SERUM FOR MEASLES

The production of animal serum for measles prophylaxis and therapeusis is the natural outcome following the use of human convalescent serum, for it is obvious that human convalescent serum can never be commercialized. Perhaps the first attempts at practical application of animal serum were made by Degkwitz [130] in Germany beginning about 1921, although the publication of his experiments in professional papers was not made until 1926. Degkwitz infected monkeys and sheep repeatedly with filtrates from the nasopharyngeal secretion of measles patients or with tissue cultures inoculated with the virus. The serum obtained from animals protected to a certain extent children exposed to measles. It failed completely when given on the first or second day of incubation. The best results (protection of 122 of 134 children inoculated) were obtained when the injection was given between the seventh and eleventh day. This is the point of difference between the animal serum and the serum of convalescent persons, the latter giving the best results when injected before the fourth day of incubation. Weise [131] used Degkwitz animal serum in a sanatorium for tuberculous children; he emphasized

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129. Keller, W., and Moro, E.: The Theory of Measles as a Reactive Disease, Klin. Wchnschr. **4**:1719 (Sept. 3) 1925.

130. Degkwitz, R.: Spezifisches Masernschutzserum vom Tier, München. med. Wchnschr. **73**:181 and 248 (Jan. 29) 1926; abstr., J. A. M. A. **86**:1174 (April 10) 1926.

131. Weise, O.: Erfahrungen mit dem neuen Masern-Tierserum nach Dagkwitz, München. med. Wchnschr. **73**:184, 1926; abstr., J. A. M. A. **86**:1174 (April 10) 1926.

early administration, and found that when given later, the serum produces a mitigation of the disease. Glaser, Hagen [132] and Progulski and Redlich [133] had little success in the use of Degkwitz animal serum. By far the greater number of investigators who experimented with this serum obtained rather indefinite results or failed completely in their attempts to protect their patients. Kaupe [134] saw a large number of children who had received injections and who developed severe serum sickness. Kochmann [135] experienced severe attacks of measles, complications with otitis and bronchopneumonia and even death in children into whom animal serum had been injected. Mosse [136] did not obtain favorable results and the children went through the typically severe course of measles in spite of serum, as did Schmidt,[137] de Rudder,[138] Anderson [139] and Seligmann, Dingmann and Alterthum.[140]

According to Schlossmann,[141] Degkwitz introduced his animal serum to the trade without conclusive scientific confirmation; he also ignored the numerous published reports of unfavorable results of the use of his serum. Moreover, it seems certain that Degkwitz first published articles concerning his animal serum in lay papers without giving any definite and detailed account of the method of producing the serum, for in the course of the five years which elapsed between 1921 and 1926, no professional paper ever brought out any item enabling other authors to make corresponding studies of the new serum. Schlossmann declared that "for the sake of German science it is necessary to compromise Degkwitz for bringing out an expedient without giving detailed and clear information concerning its origin, so that no one was able to test the method of the production."

Contrary to the method by which Degkwitz attempted to gain publicity in the introduction of animal serum, Tunnicliff and Hoyne,[142] in

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132. Hagen, W.: Praktische Erfahrungen mit dem Hammelschutzserum gegen Masern, Deutsche med. Wchnschr. **52**:871 (May 21) 1926.

133. Progulski, St., and Redlich, F.: Ueber den Wert des neuen Schutzserums nach Degkwitz, Klin. Wchnschr. **5**:1461 (Aug. 6) 1926.

134. Kaupe, W.: Med. Klin. **22**:213 (Feb. 5) 1926; abstr., J. A. M. A. **86**:1173 (April 10) 1926.

135. Kochmann, R.: Deutsche med. Wchnschr. **52**:565 (April 2) 1926.

136. Mosse, K.: Klin. Wchnschr. **5**:708 (April 16) 1926.

137. Schmidt, W.: Deutsche med. Wchnschr. **52**:1303 (July 30) 1926.

138. de Rudder, B.: Klin. Wchnschr. **5**:1406 (July 30) 1926.

139. Anderson, M. S.: Ugesk f. Laeger. **88**:1190, 1926.

140. Seligmann, E.; Dingmann, A., and Alterthum, H.: Deutsche med. Wchnschr. **52**:1220 (July 16) 1926; abstr., J. A. M. A. **87**:1164 (Oct. 2) 1926.

141. Schlossmann, A.: Klin. Wchnschr. **5**:1824 (Sept. 24) 1926.

142. Tunnicliff, R., and Hoyne, A. L.: Further Studies on a Diplococcus from Measles: Prevention of Measles by Immune Goat Serum, J. Infect. Dis. **38**:48 (Jan.) 1926.

this country, showed that the serum of a goat convalescing from a reaction produced by the inoculation of green-producing measles diplococci protected rabbits against a subsequent injection of infective material from measles. Convalescent goat serum protected human beings against measles as effectively as convalescent human measles serum when injected on the first and second days after exposure to measles. In a later publication,[143] these authors described attempts to produce serum of more highly immunized goats and to determine the prophylactic and therapeutic titers. They concluded that children receiving from 4 to 6 cc. of this serum on or before the fourth day of exposure were protected in 97 per cent of cases, whereas those receiving the same dosage after the fourth day of incubation were protected only to the extent of 45 per cent. Hoyne and Gasul,[144] furthermore, employed this Tunnicliff goat serum in the Cook County Hospital in thirty-nine cases in which the patients had been exposed to measles; thirty-four were protected, while five developed measles in a mild form. They noted that the passive immunity conferred by this method lasted from two to four weeks, and no ill effects were seen.[145] The most recent endeavor to produce animal serum is that of Tunnicliff and White,[146] who described the production in the horse of a specific immune serum by the employment of a green-producing measles diplococcus of Tunnicliff, according to the method of Dochez. This serum has been concentrated, and when tested in both unconcentrated and concentrated states was found to contain opsonins and to produce neutralizing and protective effects specific for this diplococcus. Administered by injection into children previously exposed to measles infection, it apparently gave complete protection in a few cases, incomplete protection in some and no protection in others. Further clinical tests are being made with this concentrated serum.

SUMMARY AND CONCLUSIONS

The review of the literature on experimental aspects of measles may be summarized briefly as follows:

143. Tunnicliff, R., and Hoyne, A. L.: Prevention of Measles by Immune Goat Serum, J. A. M. A. **87**:2139 (Dec. 25) 1926.

144. Hoyne, A. L., and Gasul, B. M.: Measles Prophylaxis, J. A. M. A. **87**: 1188 (Oct. 6) 1926.

145. Since this paragraph was written, another report of the use of goat serum has been made by Halpern, L. J.: J. A. M. A. **90**:1109 (April 7) 1928, who injected 5 cc. of Tunnicliff's goat serum intramuscularly into fifty children, time of exposure varying from one to six days, and the dose doubled if exposure is more than four days. He obtained complete protection in 63 per cent of cases, and mitigation of measles in 37 per cent of the patients who developed the disease.

146. Tunnicliff, R., and White, B.: An Anti-Measles-Diplococcus Serum, Boston M. & S. J. **197**:272 (Aug. 18) 1927.

1. Measles is gaining a place of greater importance as a cause of mortality in young children, and hence its control, not by mechanical methods of isolation and disinfection, but by biologic means, becomes a problem of utmost importance.

2. The bacteriology of measles has been studied by many able workers, who have considered a great variety of micro-organisms as maintaining a causative relationship to the disease; the most probable bacterium seems to be a form of coccus, diplococcus or short-chain streptococcus, as described by Tunnicliff, Caronia and Ferry and Fisher. The contention that the disease is produced by some form of filtrable virus, as emphasized by Park and Degkwitz, cannot be upheld without further study.

3. Measles has been experimentally produced by inoculation of infective material, blood, nasopharyngeal secretion and tissue cultures into man and animals, although it still remains an open question whether inoculated measles is a truly typical disease. In almost all cases of so-called successful inoculation, the disease assumes a modified or attenuated form.

4. The convalescent serum taken from seven to nine days after defervescence from patients with measles seems to contain sufficient measles antitoxin to cause successful protection in the majority of susceptible children, if given on or before the fourth day of incubation in doses varying from 2.5 to 10 cc. If complete protection is not obtained, the disease appears to be much attentuated. The duration of passive immunity thus conferred is of short duration, varying from six weeks to six months.

5. Attempts at active immunization against measles have been made, but there is not as yet any definite conclusion as to the method and final results.

6. Convalescent serum has been employed in the active treatment of a few patients with malignant measles; when a large amount of the blood is used, as in transfusion, the effect seems to be beneficial.

7. Of the immunologic observations in the study of measles immune serum, the specific skin test in the form of localized reaction at the site of injection of measles virus, as brought out by Blake and Trask, and the so-called inhibition phenomenon as observed by Debré and others, are the most interesting. These observations must be confirmed by further experimentations.

8. On account of the limitation of human convalescent serum in point of adequate supply, an endeavor is now being made, chiefly by Tunnicliff and her associates, to produce concentrated animal serum for general use. Of the various animals so far tested, goat serum seems

to offer the least amount of reaction, although the present tendency is to produce such serum in the horse as is done for other infectious diseases.

FUTURE PROBLEMS

1. There is a vital need for more conclusive work on the bacteriology of measles.

2. An urgent necessity is the production of a concentrated antitoxic serum on a large scale for universal use after determination of the prophylactic and therapeutic titers with greater accuracy.

3. From the standpoint of public health, it is of paramount importance to discover a routine method of active and passive immunization in young children, especially in children for whom an attack of measles is likely to be serious.

FELIX WÜRTZ

1518-1574 OR 1576

JOHN RUHRÄH
BALTIMORE

Felix Würtz, of Basel, a surgeon of more than ordinary gifts, worthy of mention with Ambroise Paré, friend of Conrad Gesner, the Pliny of Germany and Paracelsus the iconoclast, wrote the most remarkable treatise on children that appeared in the sixteenth century. It is, indeed, the best book of its kind up to that time, and few pediatric writings of even later date compare with it in charm and simplicity of diction or in sound common sense.

His father was a surgeon and young Felix was sent to Nuremberg to study; after that he returned to devote his days to the people of his native city.

He is best known for his book on surgery, which he called "Practica der Wundartzney, darin allerlei schädliche Missbräuche des Wundartzes abgeschaft wurden, etc." This appeared in 1563 and had a deservedly marked success. There were numerous editions in German and it was translated into Dutch, French and English. Würtz knew much about anatomy, and it must be remembered that many surgeons of his day knew little; he knew disease clinically and was familiar with pyemia, wound diphtheria, traumatic fever and healing by first intention. He knew much more than mere surgery. He knew the value of the general care of the patient; he knew the value of diet and of nursing. He wrote in no uncertain terms of the many surgical abuses of the day. The modern surgeon would find his book good reading.

Baas says that his pediatric contribution was written by his son Rudolph, but it is not clear on what this opinion is based. If it is so, then the mantle of the father found worthy shoulders in the son. It is Felix Würtz all over. He entitled it:

THE CHILDREN'S BOOK
of
FELIX WÜRTZ

A famous and expert Surgeon.
This Book was never published till now.
Treating of infirmities and defects of new-born Children;
and of the faults and abuses, which wet or dry Nurses
commit among and against little Children; and
of medicines and Cures, of such Children
which received hurt in that way.
Written for young Surgeons, wet and dry Nurses,
Maid Servants, and other parties, to whose
trust and overlooking little Children
are committed.

It was printed along with the surgery, and the English edition was transplanted from the Dutch by Lenertzton Fox, a surgeon of Zaerdam. The work is rare and inaccessible in the original, but the text of "The Children's Book" will be found in its entirety in "Pediatrics of the Past." In reviewing this work, H. L. Mencken made the following comment:

> There is a great friendliness in some of the old authors. They were not as scientific as they might have been, but the sweet went with the bitter: they actually loved children, and tried earnestly to help them. Würtz's book, which got into English soon after the German original appeared and was many times reprinted, was one long plea for mercy to the little angels. He protested against torturing with the tight bandages of his time, he urged eloquently that they be rescued from boozy and careless wet-nurses, and he rose to lyrical heights in denouncing some of the doses that grandmothers poured into them. His last words were a caution against letting flies feast upon them. "Let all be to God's glory," he concluded, "and the good of children. Amen."
>
> A noble old fellow, and certainly not unlearned. He was by trade a surgeon, and cut off many a leg with the patient strapped to a shutter, but his chief joy seems to have been found in dealing with babies.

No proper estimate of "The Children's Book" can be made in a few lines. It is so full of common sense and so bitter against the common abuses of the day. Würtz knew that thrush was communicated by nurses when washing the mouths of infants, and he advised that the mouth be let alone. He had excellent ideas on nurses and their behavior, and he knew and described how a child should be cared for and bathed. He knew much about orthopedics and the application of splints and such devices.

The following excerpt will give an idea of his style:

> Now will I speak of the thrush in Children, which caused many Children starv'd, and I cured of that weakness, more than a hundred of them.
>
> For a warning, I will give a hint of the faults committed by Nurses, in their rude manner of washing Childrens mouthes, whereby they do and have causes this great mischief unto Children.
>
> Some indiscreet people take wool, or rough linen, or the bath cloth out of the bath, feel with it to the throat, and so wash it saying how furr'd is this Child in the throat, I must wash off that white stuff, and rub it so hard that they pull off their subtile skin, even as a soft rind is peeled off the tree, which if once done, then the next day his mouth groweth more white, which if they see it, then they feel further into the mouth, and fall on washing of his mouth, saying, this Childs tongue looks white, I must scrape his tongue, and scrape and wash away the tender skin of his tongue, and make it bleed, which surely causeth the thrush in the mouth, and the more they go on in their washing, the worse they make it. This great fault about the mouth washing, hath moved me to write this Treatise, and I intreat all good people not to make use of such washing, and to warn others from it also; for the tongue doth cleanse itself, being a member which is still in motion, and groweth not weary.

An Experimental TREATISE of

SURGERIE,

In Four Parts.

1. The first Part shewing the dangerous Abuses committed among the Modern Surgeons.
2. Of Cures of all sorts of Wounds in Mans Body, from the Head to the Toe, and of other Infirmities belonging to Surgerie; how the same ought to be observed according to the Fundamentals of Art, to be handled and cured.
3. Of the Symptomes of Wounds, how they are to be discerned and known before they appear, what they foretell, how to prevent them, and how to cure them when apparent, &c.
4. Treating of all kinds of Balmes, Salves, Plaisters, Oinuments, Oyles, Blood-stenchers, Potions, Tents, Corrosives, &c. which are used for Wounds, and have been mentioned hitherto in the former Parts of this Book; how they are to be Artificially prepared, and used well. All which are very plain, and easie to be understood and managed, by an ordinary capacity.

By that most famous and renowned Surgeon, FELIX WURTZ, Citie Surgeon at *Basell*. The praise of whose worth you may read in the following Epistles, the worth it self in this Book.

Exactly perused after the Authors own Manuscrip, by *Rodolph Wurtz*, Surgeon at *Strasburg*.

Faithfully the second time Translated into *Neather Dutch*, out of the twenty eighth Copy printed in the *German Tongue*, and now also *Englished* and much corrected, by ABRAHAM LENERTZON FOX, Surgeon at *Zaerdam*.

Whereunto is added a very necessary and useful Piece, by the same Author, called the CHILDRENS BOOK; Treating of all things which are necessary to be known by all those, to whose trust and overlooking, little Children are committed.

London, Printed by *Gartrude Dawson*, over against the *Black Horse* in *Aldersgate Street*, and are to be sold at the Book-sellers Shops. 1656.

Title page of the English translation of Felix Würtz' "Treatise of Surgerie" which contains his "Children's Book."

It may be objected, why should not Children be washed in their mouthes, if filled up with slyme, and to take away that filth?

I answer, this reason is produced onely by ignorant people, which neither know, nor can distinguish, what this slyme, slabber, or skin is: what wonder? if they cannot discern it in aged people, how should they be able to discern it in Children, in whom it may sooner be discerned than in aged people, and is a great deal more dangerous in aged people, than in little Babes.

It is known among judicious people, that every new born Child, if sound, is pale and white in the throat, and if it be red or green in the throat, then is it hurt or wounded, and his cheeks and tongue are yet white, especially on the middlemost streak, what need then to have it scraped, washed or rubbed, to make it red?

Sometimes there rise blisters on the tongue, and also on the cheeks within, and at the throat; of these I do not speak now, but if a Mother or a Nurse knoweth whether they are blisters or no, as many of such were brought to me, which were tampered too long withal, insomuch that their mouthes stunk, and could neither eat nor drink: therefore care must be had to be sure whether it be the beginning of a thrush, or whether it be a defect the Child brought into the world; for if their mouthes stink strongly, then is it not natural, but comes from putrifaction and filth: for such I do not szy, that no remedies should be used; but I speak of those, which scrape and rub Childrens mouthes so long, till they have pulled off that little skin, whereby is caused the thrush.

News and Comment

APPOINTMENT OF DR. WEECH

Dr. Alexander A. Weech, Baltimore, is to spend a year in teaching in the Union Medical College, Pekin, China, as associate professor of pediatrics.

PROMOTIONS AT UNIVERSITY OF CHICAGO

The University of Chicago announces the following promotions: Dr. Charles K. Stulik as assistant clinical professor, department of pediatrics, Rush Medical College, and Dr. William L. Buhrman as clinical instructor, department of pediatrics, Rush Medical College.

CHANGES AT WESTERN RESERVE UNIVERSITY SCHOOL OF MEDICINE

Western Reserve University School of Medicine announces the appointment of Dr. Alfred T. Shohl as associate professor of pediatrics, and the following promotions: Dr. James D. Pilcher, assistant professor of pediatrics; Dr. John A. Toomey, assistant professor of pediatrics; Dr. Norman C. Wetzel, senior instructor in pediatrics; Dr. Charles L. Ruggles, senior clinical instructor in pediatrics, and Dr. Joyce Ian Hartman, as instructor in pediatrics.

CHILDREN'S AVENUES IN TOKYO

In Tokyo, 2,500 children were killed and injured by street accidents last year. The municipal authorities have decided that 200 children's avenues shall be established in the city, wherein traffic is to be stopped in order to allow children to play from 1 to 5 p. m. after school every day.

DEATH OF PROFESSOR SUMMERS

Charles Lee Summers, professor of pediatrics at the University of Maryland School of Medicine, died on July 15.

TRAINING COURSE FOR TEACHERS OF CRIPPLED CHILDREN

A training course for teachers of crippled children is being sponsored by the Missouri Association of Occupational Therapy in cooperation with Washington University Medical School and the St. Louis School of Occupational Therapy. The course is open to any certified teacher or to any student, and may be taken in conjunction with the last two years of college work.

CLINICS FOR CRIPPLED CHILDREN IN MARYLAND

The director of the state health department plans to conduct clinics for crippled children in various parts of Maryland throughout the summer. The Maryland League for Crippled Children estimates that there are about 4,500 persons under 21 years of age who are crippled. The study of crippled children in Baltimore indicates that about half of them were crippled by infantile paralysis and about 16 per cent by tuberculosis.

Abstracts from Current Literature

Anatomy and Physiology

CONGENITAL HEMIHYPERTROPHY. M. OUGRELIDZE, Nourrisson **16**:40 (Jan.) 1928.

This congenital anomaly was observed in a girl, aged 5 months. The entire right side of the body was larger than the left. Neither side showed any abnormality. There was no hereditary precedent in the maternal or paternal ancestry. Detailed measurements are given of each side for comparison. Roentgenographs showed the bones longer and larger on the right. Examinations of the blood and spinal fluid including the Wassermann reactions were negative. The infant had a laryngeal stridor which the author feels might be explained on a mechanical basis due to the disparity in the development of the two halves of the larynx, causing the aryepiglottidean folds to be abnormally close.

It is not always easy to decide whether one is dealing with a hypertrophy of one side or a hypoplasia of the other side.

McCLELLAND, Cleveland.

Pathology, Bacteriology and Biochemistry

CALCIUM AND ULTRA-VIOLET IRRADIATION. L. T. FAIRHALL, Am. J. Physiol. **84**:378, 1928.

In dogs irradiated with ultraviolet light over long periods of time, there was a slow increase of blood calcium. The effect was less with subsequent exposure, and could not be continued indefinitely. In irradiated rats on a low calcium diet, the calcium was deposited more slowly than in normal animals. The growth of these irradiated animals was apparently normal—in decided contrast to non-irradiated animals on a similar diet—but the average calcium content was only 50 per cent of that of normal rats of the same age. On a normal calcium diet, the irradiated rats had a somewhat higher calcium content than normal rats of the same age.

H. E. EGGERS.

CHANGES IN THE PERCENTAGE OF CALCIUM AND PHOSPHORUS OF THE BLOOD FOLLOWING SECTION OF THE SYMPATHETIC, VAGUS NERVES AND SPINAL CORD. BENJAMIN N. BERG, ALFRED F. HESS and ELIZABETH SHERMAN, J. Exper. Med. **47**:105, 11, 1928.

When a splanchnic nerve or the celiac plexus was severed, a definite fall in serum calcium resulted, the level falling to 6 mg. per hundred cubic centimeters and remaining low for one or two weeks. Tetany, however, did not develop. The inorganic phosphate was slightly altered. On the other hand, when the vagi nerves were severed, the serum calcium rose. The equilibrium of both calcium and phosphorus was rendered less stable by the division of the sympathetic or the parasympathetic nerves. A marked rise and disturbance in equilibrium of the calcium in the blood was brought about by section of the spinal cord in the upper dorsal segment. This reaction, however, was not constant.

A UNIT FOR SCARLET FEVER STREPTOCOCCUS ANTITOXIN. R. E. DYER, Pub. Health Rep. **43**:1659 (June 29) 1928.

A definite amount of standard serum is suggested as a permanent unit. This unit has been selected to equal ten times the smallest amount of scarlet fever streptococcus antitoxin necessary to neutralize one test dose of toxin; but the

designated amount of serum and not the toxin dose is the final measurement of reference. The standard serum as dissolved at present contains 40 such units per cubic centimeter.

SANFORD, Chicago.

FLOCCULATION OF DIPHTHERIA AND TETANUS TOXINS WITH THEIR RESPECTIVE ANTITOXINS. S. SCHMIDT, Ann. de l'Inst. Pasteur. **42**:63, 1928.

In a certain mixture of tetanus toxin and antitoxin there is ordinarily formed a flocculation as reported by Ramon. This flocculation does not always appear with the same regularity and is not always indicative of the neutral point of mixture as is the case with diphtheria toxin and antitoxin.

The determination of the antigenic power of a toxin may, in certain cases, be effected by the flocculation method as indicated by Ramon and Descombey. In the author's experience, it was necessary to control each time the in vitro tests by injecting the flocculated mixture into animals.

The titration of antitetanus serum may be effected to a fair approximation with a great number of serums; the author agrees with the report of Abt and Erber.

Certain serums and certain toxins have several zones of flocculation. The method of titration in vitro may be employed (especially in the titration of toxins) only if one has found serums reacting in the same way with all toxins.

Certain antitetanus serums show a concordance between the rate of flocculation and the rate of neutralization. The rate of flocculation may indicate the avidity of antitoxin for toxin, but this avidity is not indicative of the antitoxic potency of the serum and is determined by the person furnishing the serum.

AUTHOR'S SUMMARY.

ALLERGY AND ALLERGIC DISEASES. R. ROHRBACH, Dermat. Ztschr. **51**:424 (Jan.) 1928.

Rohrbach discusses the old and the new conceptions of anaphylaxis, allergy and idiosyncrasy. It has been shown that anaphylactic shock can occur without previous sensitization and that idiosyncrasy can be acquired. Allergy is now regarded as a congenital or an acquired property of specific reaction against definite, widely varying substances that, in the same doses, are harmless to the normal organism. Not only proteins but lipoids have antigenic properties. Furthermore, substances which alone are not antigens can acquire antigenic function with the assistance of certain substances that the organism itself can supply. The general clinical symptoms of all diseases originating in an allergic mechanism are temperature variations (particularly fall), lowered blood pressure, collapse, shock and cerebrospasm. The skin symptoms are itching, formation of wheals, inflammation and hemorrhages. Symptoms showing the involvement of the mucous membranes are sneezing, coryza, inflammation, connective tissue catarrh, bronchial spasms, vomiting and diarrhea. In the blood there is a sudden fall in the number of leukocytes, eosinophilia and leukopenia; in the vascular system, vasomotor paralysis, local dilatation of the vessels and exudation. The allergic diseases are frequently first diagnosed from the allergic symptoms. There are a number of disease conditions of the skin for which the paroxysmal appearance of an allergic symptom complex is characteristic, in which symptoms affecting the capillaries and the organs containing smooth muscle are particularly common. The dependence of these phenomena on an allergen is demonstrable in many cases, but in others it is only probable. For the exact diagnosis, a detailed history should be obtained and the skin reactions should be tested with extracts of various substances. In evaluating the results, the possibility must be borne in mind of a group sensitiveness to a number of extracts and also that the capacity for reaction varies in different regions of the skin. In the decomposition of proteins, poisonous substances with anaphylactic action, so-called shock poisons, arise. The most powerful are the cyclic diamines. The most important of these is

histamine. It is present in ergot and in pituitary, also in Witte's peptone. Almost all of the allergic symptoms may be caused by histamine. The skin is the chief site of allergic processes. Urticaria, eczema and Schönlein-Henoch's purpura are definitely allergic diseases. Urticaria is the most frequent symptom of an allergy against foodstuffs. Witte's peptone or minimal quantities of the injurious food itself, given before the meal has been found to prevent the urticarial attack. In many cases, eczema represents the type of an allergic dermatosis. In the true eczematous subject, the capacity of developing eczema rests on a basis of cellular allergy and is entirely distinct from the capacity found to exist in normal subjects to react with an acute superficial dermatitis to chemical, mechanical and physical noxae given in excessive doses or over a long period of time. Healthy skin of eczematous subjects is seven times as sensitive as that of normal persons. Persons who never have had eczema, but who react positively in this respect, must be regarded as having a latent eczema. In 75 per cent of such persons, the idiosyncrasy is monovalent. If the eczema becomes manifest in consequence of continual sensitization, the specificity of the idiosyncrasy is lost, and various, often insignificant, noxae are able to excite or exacerbate the eczema. The exudative early or late eczema in status exsudativus is the type of such an allergic eczema. Characteristic of this condition are heightened purine metabolism, decreased capacity to bind salicylic acid and a positive reaction to human cutaneous scales. Because of this capacity for developing multiple sensitiveness that is found in patients with constitutional eczema, it is wise to avoid the use of all provocative remedies in giving treatment. Many therapeutic failures may be explained from the fact that at the beginning preparations containing sulphur, salicylic acid, ammonium sulphoichthyolate or resorcinol were used and fresh injurious influences were thus brought to bear on the plurivalent hypersensitiveness. If formation of wheals accompanies the eczema, alimentary allergens—fish, egg albumin, cow's milk, rice, potato, etc.—should always be thought of. Alimentary allergens show a preference for the subcutaneous connective tissue and the vessels of the cutis. Noxae attacking from the outside affect chiefly the epithelium and capillary bodies.

CARPENTER, Chicago.

THE EFFECT OF SUN THERAPY ON THE DUSTLIKE PARTICLES OF THE BLOOD. GIUSEPPI GELLI, Monatschr. f. Kinderh. **39**:1, 1928.

It is known that observation of a fresh specimen of blood under the dark field shows tiny particles of a bullet or dustlike form which are about one micron in diameter and in great numbers. They were first considered as tiny particles of fat. Others have ascribed them to breaking down of red blood corpuscles. In a study of four children with anemia and treated with ultraviolet therapy, the writer found these blood particles diminished proportionately to the improvement of the anemia. At the same time, there was an increase in the particles after meals. The writer believes two influences are at work. An alimentary factor increases the particles of fatty nature. Distintegration of the blood corpuscles or possible products of tissue catabolism supplies the remainder of this blood débris.

HELMINTHIASIS WITH SPECIAL REFERENCE TO CHILDHOOD. HERMAN BRUNING, Monatschr. f. Kinderh. **39**:72, 1928.

Bruning gives a complete review of the literature for the years 1926-1927, including all the contributions to pathology, diagnosis, symptoms, complications and treatment.

In general, echinococcus is rare. In Finland, one fourth of the population is infected with *Bothriocephalus latus*. The worms are found much more frequently in rural than in urban populations. Again, they are much more frequent in asylums in which children are crowded together. In the long list of reports, one is astounded at the frequency with which the commoner types of worms are found throughout the population of rural and institutional Europe. In some statistics,

including a study on 1,300 children, 74 per cent were infected with the commoner parasites such as *Trichocephalus, Ascaris, Taenia saginata, Taenia nana* and *Oxyuris.*

As regards diagnosis, it is considered wiser to repeat the examination for eggs after an interval of eight days. Of all the technics recommended, the writer found that of Fullerborn the best, but unfortunately he does not describe the method. For *Oxyuris,* one should not forget to seek eggs in the folds of the skin around the anus. Eosinophilia is always a valuable sign. Some of the writers got favorable results with skin tests.

The symptoms and complications reported would fill a textbook. The treatment consists of the same remedies commonly in use. At times, the author got better results by introducing them directly into the duodenum.

ALIMENTARY INTOXICATION IN ANIMAL EXPERIMENT. S. ROSENBAUM, Monatschr. f. Kinderh. **39**:121, 1928.

In young dogs, cats, apes and rabbits, exsiccation does not lead to the typical picture of alimentary intoxication. The deep breathing, particularly, is absent. The injection of endotoxins also does not produce the picture. The combination of the two factors, however, is effective. When animals are made to lose more than 13 per cent of their body weight, and at the same time an injection of fresh toxin, obtained from organisms such as colon bacilli, is made in a dose of 3 mg. per kilogram of body weight, typical alimentary intoxication often develops. The effect of the endotoxin on the exsiccated animal does not cause a further increase in water loss or a further exsiccation of any particular organ.

GERSTLEY, Chicago.

Nutrition

THE ANTIRACHITIC EFFICIENCY OF WINTER SUNLIGHT OF WASHINGTON, D. C. CAPTAIN W. D. FLEMING, Mil. Surgeon **62**:592 (May) 1928.

During December, January, February and March in Washington, D. C., there was sufficient ultraviolet light to promote normal calcification in rats confined under a glass permeable to this light. Their diet was markedly rachitic, as rats on the same diet and not thus exposed were rachitic. The rats that were irradiated also showed a greater gain in weight than those of the control group. The authors conclude that the construction of a solarium would be of advantage in the winter in this locality.

SANFORD, Chicago.

THE EFFECT OF OBSCURE MASTOIDITIS UPON NUTRITION IN INFANCY. S. W. CLAUSSEN, New York State J. Med. **28**:23 (Jan. 1) 1928.

In thirteen of twenty-five patients with severe diarrhea, masked or obscure infection of the mastoid was found. Local symptoms were absent, but otitis media was usually present. In two cases not showing involvement of the mastoid, infection of the nasal sinus was found. Of a group of patients with mastoiditis under 2 years of age, cholera infantum was present in thirteen. Two patients had marked vomiting and loss of weight, and eight had chronic malnutrition.

Of twenty-two patients with otitis media, eight had severe diarrhea and desiccation which improved after drainage had been established. While the writer does not claim that all cases of diarrhea and malnutrition are due to otitis media or to mastoiditis, he does believe that in every case of severe diarrhea with desiccation these conditions should be seriously considered. The most important local signs suggesting mastoiditis are: (1) otitis media, even with slight grayness of the drums; (2) sagging of the posterior superior wall near the drum; (3) enlarged glands over the mastoid. The x-ray has been of little value except in children over 6 months of age.

Forty-five per cent of the patients with cholera infantum recovered after operation. As the patients were all profoundly ill, the mortality was not considered unusually high. All of the patients with malnutrition recovered after operation.

AIKMAN, Rochester, N. Y.

THE COMBINATION OF NURSING AND PREGNANCY. HERBERT STUX, Monatschr. f. Kinderh. **38**:481, 1928.

Up to the present there have been insufficient studies made to give any real information as to the effect of nursing on pregnancy, and vice versa. A careful study must include (1) the influence of lactation on the fetus; (2) the influence on the condition and development of the nursling; (3) the influence of pregnancy on lactation; (4) the influence of pregnancy on the composition of breast milk and (5) the influence of these factors on the health of the mother.

In a study of fifty cases from these points of view, the writer does not give definite conclusions. The only striking observation was a noticeable diminution in the quantity of breast milk in the first few months of pregnancy.

EXPERIENCES WITH A FAT-GRUEL FEEDING. GUSTAV JUNGWIRTH, Monatschr. f. Kinderh. **38**:500, 1928.

The success of Czerny's butter-starch feeding as well as Moro's butter-flour-milk mixture led Knoepfelmacher to try an even more concentrated feeding. His mixture consisted of 130 Gm. of milk, 10 Gm. of flour, 10 Gm. of butter and 15 Gm. of sugar, boiled down to 100 Gm. In contrast to Czerny's mixture, which contained 85 calories, and Moro's mixture, which contained 160 calories, 100 cc. of Knoepfelmacher's mixture represents 260 calories. A number of children were kept on this diet with one or two feedings a day for more than seven weeks. The diet is indicated in marked dystrophy and in some cases of pylorospasm. Many children did well on the diet. The advantage is its high caloric content.

GERSTLEY, Chicago.

CHOLESTERIN THERAPY IN RICKETS. H. VOLLMER, Ztschr. f. Kinderh. **44**:87 (Aug.) 1927.

By percutaneous administration daily for two weeks of from 2.5 to 3 Gm. of irradiated cholesterin dissolved in chloroform-paraffin oil, the metabolism of healthy infants was influenced in an antirachitic sense. The secretion of acids was much increased in the urine and the total acid quotients raised. Irradiated cholesterin given in the form of zwieback was able, without any other form of therapeusis, to heal florid rickets in infants and rickets complicated by tetanus in just as short a time as direct radiation with artificial sunlight. The activity of the cholesterin was not injured either by the baking or the aging of the zwieback. For complete and prompt healing, the total amount of irradiated cholesterin in mild and moderately severe forms of rickets was about 20 or 25 Gm. and in severe rickets, from 40 to 50 Gm. Contrary to the action described in the literature of increasing the resistance by the use of cholesterin, the resistance was diminished, especially to respiratory diseases. The investigator warns of the danger in using the cholesterin of making anemia worse and of the occurrence of cholemia.

INSULIN IN THE TREATMENT OF NONDIABETIC CONDITIONS IN INFANTS AND CHILDREN. WALTER BLOCK, Ztschr. f. Kinderh. **44**:204 (Aug.) 1927.

In the gain in weight of dystrophic patients treated with insulin and dextrose, Block assigned the outstanding rôle to the addition of sugar. In eutrophic infants, retention of the quantity of water added did not follow, although in a number of the cases the passage of water through the tissue was slowed so that the maximum excretion came later, not in the first hours as in the normal child. In the treatment of patients with acute water loss and intoxication, an improve-

ment occurred in a number without the administration of insulin. When insulin was used, whether the disappearance of toxic symptoms and the increase in weight was dependent on insulin was doubtful, for with other treatment for these conditions the same results were observed with no less frequency. In the greater number of the patients treated with insulin, there was no success in saving the life of the child. An influence on the weight and the appetite of tuberculous or neuropathic children who did not eat was not observed, in spite of the high doses of insulin, up to 60 units daily.

EMERSON, Boston.

Prenatal Conditions

PRENATAL RUPTURE OF THE INTESTINE WITH SUBSEQUENT DYSTOCIA. JAMES HUBERT SKILES, J. A. M. A. **90**:1618 (May 19) 1928.

A case is reported in which a volvulus of the small intestine was found. In the twisted loop, there was evidence of a healed perforation. The abdominal cavity was so distended with fluid that dystocia resulted.

BONAR, Salt Lake City.

CRANIORACHISCHISIS: ITS CLINICAL AND MORPHOLOGIC ASPECTS. MARTIN S. SICHEL, Northwest Med. **27**:229 (May) 1928.

Sichel reports the cases occurring during five years in 5,911 deliveries in the Minneapolis General Hospital. There were eleven cases of craniorachischisis, or 0.2 per cent of the total deliveries, or 7.5 per cent of the stillbirths. There were eight cases of anencephalus, one case of exencephalus and two cases of meningoencephalocele.

Anencephalus and exencephalus often are associated with marked hydramnios, and can be diagnosed before birth by the x-ray. At autopsy the fetus often shows hypoplasia or complete absence of the suprarenal. Associated anomalies are frequent. Levaditi stains seldom show spirochetes, and the Wassermann reaction is usually negative. Abnormal presentations frequently occur.

SCOTT, Philadelphia.

INDUCTION OF PREMATURE LABOUR IN RELATION TO MENTAL DISEASE. R. PERCY SMITH, Brit. M. J. **1**:9 (Jan. 7) 1928.

The author presents two groups of cases, seven in which pregnancy was allowed to continue and ten in which it was terminated before viability of the child. The first group shows how acute insanity may run its course during the whole of pregnancy and yet recovery may result. The mental condition of four of the patients improved during the pregnancy and before parturition. The author concludes that only purely medical considerations should be allowed to weigh in deciding as to the termination of pregnancy, and quotes several opinions in support of his belief.

CONGENITAL AND ACQUIRED ABNORMALITIES OF THE PULMONARY ARTERY. R. C. CLARKE, C. F. COOMBS and G. HADFIELD, Quart. J. Med. **21**:51, 1927.

The object of this report is to confirm the view that there are syphilitic and nonsyphilitic abnormalities of the pulmonary artery and to advance the idea of a probable inherited etiologic factor in connection with the latter. Dyspnea and cyanosis were prominent symptoms in the five patients who eventually came to autopsy. The syphilitic type was represented in a woman, aged 39, who had shortness of breath and cough for three years before death, and whose body was the seat of a generalized syphilitic arteritis, manifested in the lungs as an obliterating endarteritis accompanied by a gross perivascular pulmonary fibrosis. The primary, nonsyphilitic type of pulmonary sclerosis occurred in a woman, aged 22. The condition was most pronounced in arteries from 7 to 3 mm. in diameter,

as acellular, nodular intimal thickenings devoid of inflammatory reaction. A congenitally wide pulmonary artery, twice the size of the aorta, was found in a girl, aged 10 months, dying of bronchopneumonia; and an interventricular septal defect, an anatomically patent foramen ovale and a generalized dilatation of the pulmonary artery and its branches were seen in a boy, aged 6 months, who died suddenly. A girl, aged 6 years, had marked atheromatous changes in her pulmonary arterial system, and her family history was carefully investigated. The father died at the age of 47, from rheumatic heart disease; one sister died at the age of 3½ years of bronchopneumonia; another died at the age of 1½ years after bronchitis; one brother died at the age of 8 months of bronchitis; another drowned at the age of 20 months. A 4 year old sister had had dyspnea and cyanosis for two years and had been closely observed since the onset of the symptoms.

PETERSEN, Montreal.

DOLICHOSTENOMELIA. A. ZUBER, Nourrisson **15**:292 (Sept.) 1927.

Dolichostenomelia is a congenital anomaly in which all the bones of the body are elongated. The deformities are most conspicuous in the hands and feet, making them appear extraordinarily long and slender, though the author presents measurements to show that the long bones are also involved. Marked muscular wasting accompanies the disorder.

The first case of this sort was described by Marfan in 1896. Dubois of Liége was able to collect reports of about twenty cases from the literature showing its rarity. There is frequent association with other congenital malformations: congenital dislocation of the hip, webbed toes, congenital heart disease and dislocation of the crystalline lens with a high degree of myopia. The author's case showed a bifid uvula and nystagmus.

The cause of the condition remains obscure. Tuberculosis and syphilis have been excluded. X-ray studies have shown an abnormal development of cartilage referred to as a hyperchondroplasia.

MCCLELLAND, Cleveland.

DEMONSTRABLE IRON IN THE LIVER AND SPLEEN OF FETUSES AND NEW-BORN BABES. P. BOECKER, Centralbl. f. allg. Pathol. u. path. Anat. **41**:193, 1927.

From a review of the literature, the author concludes that examination of the liver and spleen usually discloses the presence of iron; and fluctuations in the amount of iron during intra-uterine and postuterine life seem to follow the same physiologic rules in humans and animals. In all, he examined sixty persons, whose ages were between 1 month (intra-uterine life) and 48 hours (postuterine life) at full term. Syphilitic patients were excluded. The Berlin blue and Hueck's modification of Turnbull's blue reaction were used as a means of studying the iron deposits. In the liver, the iron granules were found in the Kupffer's cells, liver cells, perivascular tissues and, at times, in the lymph spaces. In the spleen, the greatest deposits were in the sinus epithelium and perivascular tissues. Graphically represented there was a slow increase in iron in both organs during the first three months of intra-uterine life, when a rapid increase to three times this amount in the fifth and sixth months, a drop to a median position in the seventh and eighth months and again a rapid rise in the ninth and tenth months. It is suggested that these waves of iron deposition are related to the action of the liver, spleen and bone-marrow in the formation of blood.

GEORGE RUKSTINAT.

LIGATION OF THE INTERNAL CAROTID ARTERY IN REPEATED HEMORRHAGE OF THE EAR FOLLOWING RADICAL OPERATIONS. EUGEN CHARSCHAK, Ztschr. f. Hals-, Nasen- u. Ohrenh. **19**:393 (Dec. 22) 1927.

Hemorrhages from the ear canal following a lesion in the wall of the carotid are rare. Up to 1918, forty-two cases had been reported, all with a fatal outcome. Most of the patients were tuberculous. Death results within four or five minutes, if a physician is not present to exercise strong pressure on the common carotid artery and pack the ear canal. These measures are not always

successful. Therefore, ligation of the common or the internal carotid is necessary. Hessler thinks that ligation of the internal carotid artery is not sufficient. Charsckak reports a case in point. A woman, aged 43, had developed suppuration of the ear, after typhus, five years previous to examination. On January 31, a radical mastoid operation was performed. On February 19, a sequestrum was found located farther to the front. An attempt was made to remove the sequestrum, and a severe arterial hemorrhage resulted. Tight packing stopped the hemorrhage. Another hemorrhage occurred on February 23, and a third on March 17. Under local anesthesia the internal carotid artery was tied within a few hours. The patient recovered. The internal carotid artery was not ligated after the first hemorrhage because the good effect of packing by way of the external meatus had created false hopes.

AMBERG, Detroit.

PURULENT DOUBLE KIDNEY IN CHILDHOOD. G. LANGE and A. MYERSTEIN, Ztschr. f. Kinderh. **44**:218 (Aug.) 1927.

The term "double kidney" means two kidneys completely separated or attached to one another by connective tissue on one side of the body in the normal position of the kidneys, or a second double kidney on the other side of the body. Double kidney occurs more frequently on one side than it does on two sides and is found more frequently on the left than on the right side. It may not cause inconvenience and may be discovered first at postmortem examination. The upper kidney is frequently more altered pathologically than the under one. Each kidney possesses a pelvis and a ureter, but the ureters may unite with one another distally or they may run separately to the bladder. In many cases one will open somewhere in the urogenital tract; for example, in the vagina in the female or the seminal vesicle in the male. Two instances of one-sided purulent double kidney are reported by Lange and Myerstein. One was in a girl, aged 6 months, and gave a picture of chronic, intermittent pyonephritis; in the other patient, a boy, aged 6 years, a diagnosis of appendicitis was made. Both children were cured by excision of the diseased double kidney.

EMERSON, Boston.

Diseases of the New-Born

ICTERUS NEONATORUM GRAVIS: REPORT OF A CASE WHICH RECOVERED WITH SEQUELAE POINTING TO AN INVOLVEMENT OF THE CENTRAL NERVOUS SYSTEM. HARRY M. GREENWALD and WILLIAM MESSER, Am. J. M. Sc. **174**:793 (Dec.) 1927.

Greenwald and Messer report a case of malilial icterus neonatorum gravis with recovery. The first two infants of the same mother suffered with this disease, with fatal termination. The symptoms in this case which pointed to the involvement of the central nervous system, as evidenced by spastic diplegia and idiocy developed subsequently.

HENSKE, Omaha.

THE PREVENTION AND TREATMENT OF ASPHYXIA IN THE NEW-BORN. YANDELL HENDERSON, J. A. M. A. **90**:583 (Feb. 25) 1928.

Failure of the new-born to breathe or a condition of insufficient natural respiration should not be treated by the old-fashioned methods of cutaneous "stimulation."

Resuscitation of the new-born should be based on the modern conception of the regulation of respiration by the action of the blood gasses on the respiratory center. Oxygen is not a stimulant but a foodstuff. Deficiency of oxygen, beyond a first slight stimulating effect, depresses the nerve centers. In the absence of oxygen, the tissues of the body cannot produce carbon dioxide. It is the carbon dioxide carried by the blood from the tissues to the brain that is the physiologic

stimulant to respiration. When the center is depressed, it requires more than the normal amount of this stimulant to induce activity.

Compression of the head and the consequent decrease of the supply of blood to the brain during prolonged labor depress the respiratory center, so that after delivery the center does not receive a chemical stimulus sufficient to overcome this depression. Because of this condition of the center, the first cry does not occur, and the lungs remain atelectatic. In order to start respiration, a gentle inflation with oxygen and carbon dioxide for two or three seconds three or four times a minute should be applied. As soon as natural breathing develops, the inflations should be stopped, but inhalation of this gas mixture should be continued until full breathing is established. This is not only the physiologic and therefore the best method; in its essential features, it is really the only possible method that nature and science offer.

BONAR, Salt Lake City.

GOITER IN NEW-BORN INFANT. PAUL W. SWEET, Northwest Med. **27**:183 (April) 1928.

Sweet reports enlargement of the right lobe of the thyroid of a new-born infant, which was about one-fourth the size of the infant's head. The mother had a colloid goiter. She was given iodized calcium lactate, and the infant was breast fed. In nine weeks the swellings had disappeared from the necks of both the mother and the child.

DISAPPEARANCE AND REAPPEARANCE OF HEART MURMURS IN THE NEW-BORN. A. REUSS, Ztschr. f. Kinderh. **44**:225 (Aug.) 1927.

Loud systolic murmurs which are demonstrable during the first days of life may disappear later. These transient murmurs apparently are the result of the continued patency of the fetal passages as a result of some disturbances of circulation in the lungs. Likewise, in some older children in good health, it happens occasionally that distinct systolic murmurs disappear after a time. On the other hand, in a case of transposition of the great vessels with a septal defect, a systolic murmur developed only after several days.

EMERSON, Boston.

Acute Infections

THE CIRCULATORY COLLAPSE IN DIPHTHERIA. CHARLES W. EDMUNDS and FRANKLIN D. JOHNSTON, J. A. M. A. **90**:441 (Feb. 11) 1928.

The evidence at present points to the fact that fatal circulatory collapse in diphtheria is due primarily to an action of the toxin on the receptive substance of the splanchnic nerves, which produces a loss of control of the abdominal vessels by these nerves. The vessels relax and the blood pressure falls, resulting in a deficiency in the amount of blood returned to the heart. The general arterial pressure falls; this causes anemia of the medullary centers and possibly death. There is, therefore, a distributive oligemia, from failure of the splanchnics and in addition, profound myocardial changes. The importance of the latter in the functional activity of the heart is impossible to estimate.

THE PREVENTION AND MODIFICATION OF MEASLES BY MEASLES ANTIDIPLOCOCCUS GOAT SERUM. LOUIS J. HALPERN, J. A. M. A. **90**:1109 (April 7) 1928.

The measles antidiplococcus goat serum, developed by Tunnicliff and Hoyne, apparently is an effective immunizing agent against measles in a large percentage of cases. Sixty-three per cent of forty-five immunized patients, who gave a history of never having had measles, were successfully protected. While seventeen

developed the disease, the majority developed it in attenuated form. Measles antidiplococcus goat serum is both antibacterial and antitoxic. Serum reactions were not found in the entire series studied.

CONVALESCENT AND ANTITOXIC SERUMS IN SCARLET FEVER. J. E. GORDON, B. B. BERNBAUM and L. C. SHEFFIELD, J. A. M. A. **90**:1604 (May 19) 1928.

Scarlet fever streptococcus antitoxin was used in the treatment of 1,021 patients with moderately severe or severe forms of scarlet fever. In 120 patients, severely ill, convalescent serum was used. Scarlet fever streptococcus antitoxin exerts a favorable effect in reducing the severity of the febrile stage of the disease, in the course and duration of the fever, and in the extent and duration of the lesions on the skin. Complications are less frequent in patients receiving scarlet fever streptococcus antitoxins. Judged on the basis of the case fatality rate and the percentage incidence of complications, there is no essential difference between patients with severe scarlet fever treated with the antitoxin and with convalescent serum. Absence of the reactions after convalescent serum is administered makes it more desirable.

BONAR, Salt Lake City.

ULTRA-VIOLET LIGHT AND VACCINE VIRUS. THOMAS M. RIVERS, HENRY STEVENS and FREDERICK L. GATES, J. Exper. Med. **47**:37 and 45, 1928.

Rabbit skin subjected for a few minutes to ultraviolet light and then inoculated at once with vaccine virus is less susceptible to the action of the virus than is untreated skin. If twenty-four, forty-eight or seventy-two hours elapse between the time of irradiation and inoculation, the treated skin appears to be more susceptible than is untreated skin. Skin repeatedly exposed to ultraviolet light is less susceptible to the action of vaccine virus than is nonirradiated skin. Under the experimental conditions described in the present paper, it was found that the amount of energy required to kill staphylococci at single wave-lengths in the active ultraviolet region was approximately the same as that necessary to inactivate vaccine virus.

AUTHORS' SUMMARY.

METHODS OF ISOLATING A BACTERIOPHAGE FOR BACILLUS DIPHTHERIAE. JULIUS A. KLOSTERMAN and KATHRYN W. SMALL, J. Exper. Med. **47**:121, 1928.

Of the attempts to isolate an antidiphtheria phage (1) from stools collected daily during the course of a case of the disease, (2) from a 33 day old broth culture of *B. diphtheriae,* (3) from intestinal contents and peritoneal washings of guinea-pigs inoculated with three different toxic strains of *B. diphtheriae,* none yielded an antidiphtheria phage. However, of eleven specimens of feces collected from eleven antitoxin horses one was found to contain a bacteriophage active against *B. diphtheriae.* This phage was not observed in the first generation and did not show up until transferred the second time. Had the results of the first transfer been regarded as final in all certainty the existence of a phage would not have been recognized. Two additional specimens of feces from the positive horse were later tested to determine whether this bacteriophage was continually present in the intestinal tract of this animal. Both of these feces filtrates failed to yield a phage. Later, a sample of freshly collected blood serum from the same horse was tested and found not to contain a phage. The antidiphtheria phage was tested against eighteen nondiphtheria strains of micro-organisms to determine whether it would show lytic activity for related or unrelated bacteria. There was no evidence of lysis in any of these types. The specificity of this phase was also tested on nine strains of *B. diphtheriae* and found to be active on three heterologous strains (strain M 1314, strain F and strain G). These incidentally were all recently isolated. It failed to lyse the remaining six strains of which five were recently isolated. *B. diphtheriae* strain M 1314 was used in combination with nine

heterologous bacteriophages isolated from various sources, to determine if any of these phages would by chance lyse this culture. The results were all negative. To date this phage fails to show complete lysis although the twenty-second generation has a titer of 1×10^{-9}

AUTHORS' SUMMARY.

CURRENT WORLD PREVALENCE OF COMMUNICABLE DISEASES, Pub. Health Rep. **43**:1664 (June 29) 1928.

From May to June, the mortality rate for the United States dropped off rapidly from the high level of March. The death rate of sixty-seven of the largest cities was 13.3 as compared to 11.8 of a year ago. Influenza and pneumonia continued at a high level, while poliomyelitis increased. There were 102 cases reported, as against eighty-one of the previous month. The mortality rates of meningitis, smallpox, scarlet fever, diphtheria and measles showed the expected seasonal decline.

SANFORD, Chicago.

SCHICK TESTS AND RURAL IMMUNITY. PHILIP CORR, Wisconsin M. J. **27**:210 (May) 1928.

Schick tests on 169 country children, including those of high school age, showed 90.5 per cent positive reactions as compared with 25 per cent positive reactions in city children.

A review of comparative statistics shows about a 50 per cent greater incidence of disease in rural people than in city people, indicating a relative lack of nonspecific immunity.

The initial Schick test in country children should be replaced by the first dose of toxin antitoxin given subcutaneously, and subsequent injections should not be given if this modified Schick test should cause negative reactions.

JANNEY, Milwaukee.

THE HISTOLOGY OF POSTVACCINAL ENCEPHALITIS. J. R. PERDRAU, J. Path. & Bact. **31**:17, 1928.

The claim of Turnbull and McIntosh that postvaccinal encephalitis can be distinguished histologically from epidemic encephalitis is confirmed. Although comparison with poliomyelitis could not be carried out satisfactorily, owing to lack of material, postvaccinal encephalitis and poliomyelitis are probably different as regards the type of lesion. Postvaccinal encephalitis is characterized by the presence around certain vessels of the central nervous system of an area of demyelinization (the extra-advential infiltration or softening of Turnbull and McIntosh). From a study of the literature it appears that the nervous disorders complicating smallpox, measles and other fevers as well as those ocurring in the course of antirabic inoculations (Pasteur's treatment) are histologically identical with postvaccinal encephalitis and myelitis. The perivascular demyelinization of postvaccinal encephalitis is essentially similar to that found in comparatively acute cases of disseminated sclerosis. The possibility is discussed that the agent (living or not) responsible for the demyelinization in these various forms of nervous disorder may be the same for all of them.

AUTHOR'S SUMMARY.

PREVENTIVE VACCINATION AGAINST SCARLET FEVER. H. SPARROW, Presse méd. **36**:549 (May 2) 1928.

Antiscarlet fever immunization has an undeniably constant influence on the morbidity in scarlet fever. The percentage of morbidity in both immunized and nonimmunized persons decreases with age. It is influenced by the amount of toxin injected. On the average, nonimmunized persons furnish from three to four times as many cases as immunized persons of the same age.

SANFORD, Chicago.

PATHOLOGIC ANATOMY OF THE LUNG IN WHOOPING COUGH. FRIEDRICH FEYRTER, Frankfurt Ztschr. f. Path. **35**:213, 1927.

In an epidemic of whooping cough, the author studied 225 cases which came to autopsy. He found that the lungs early become involved in the course of whooping cough. Inflammation of the bronchial tree takes place early and remains permanently. These changes consist of mucopurulent endobronchitis and endobronchiolitis, high grade peribronchitis and peribronchiolitis. Bronchiolitis fibrinosa occurs often and may be followed by bronchiolitis obliterans. Bronchiectasia is common; bronchial stenosis may also be found. The peribronchitis explains the long duration and frequent exacerbations which occur in whooping cough and the peculiar sounds of the bronchial râles.

The disease of the greater bronchial tree is diffuse while severer forms of endobronchitis are unusual and come about through secondary infection. From the bronchiolitis and peribronchiolitis arises an interstitial pneumonia which remains as a small nodular peribronchial pneumonia. In many cases the interstitial inflammation passes through the alveoli causing the formation of exudate. The inflammation spreads frequently by the lymph vessels to produce other localized areas of peribronchiolar pneumonia. The areas of focal pneumonia may spread out over a limited area and become indurated or fill up the alveoli to the borders of the lobule and become chronic interstitial acinar or lobular pneumonia.

Croupous and also carnifying lobar pneumonia are not seen in cases of whooping cough. The exudate is mostly leukocytic, rarely fibrinous and then only in limited amount.

In chronic cases, vicarious emphysema is rarely seen. Changes in the pleura are in the form of fresh fibrinous pleuritis which is poor in cells; in chronic cases the pleurae are adherent. The vessels in the affected part of the lung in the chronic cases show hyperplasia of the elastic and collagen fibers in both the intima and the media. In 32 cases of 225 there were evidences of tuberculosis.

E. M. HALL.

ULCERATIVE-NECROTIC GLOSSITIS IN SCARLET FEVER. IMRE BERGER, Monatschr. f. Kinderh. **38**:289, 1928.

Berger reports the case of a child with scarlet fever in which the tonsils and later the entire mouth were covered with a thick tenacious mucus. This changed to a dirty slimy membrane involving the throat. The necrotic process extended to the soft palate. Later, the tongue was covered with ulcerating necrotic patches. Diphtheria cultures were negative. The process lasted three weeks and ended in recovery.

CLINICAL REPORT OF ONE HUNDRED FIFTY CASES OF SCARLET FEVER FROM 1923-1926. GERHARD DEMOHN, Monatsch. f. Kinderh. **38**:344, 1928.

Demohn presents a careful clinical study in which he reviews the cases of scarlet fever from practically all angles. He discusses the skin manifestations, various types of blood picture, sex, age, season, fever, pulse, urine and all the complications.

For a time he did not get satisfactory results with his Dick tests but later, when he used a toxin obtained from American strains, results were more satisfactory. The article, which is about ninety pages long, should be of especial interest to anyone making a clinical study of scarlet fever.

OVERCOMING CONTAGIOUS DISEASES IN THE CHILDREN'S HOSPITAL. OSCAR HERTZ, Monatschr. f. Kinderh. **38**:527, 1928.

In discussing measles, whooping cough, diphtheria and chickenpox in connection with epidemics in hospital wards, the writer finds that measles can be successfully overcome by proper isolation in the early stages. It is probable that measles can

be carried by well adults. Whooping cough causes the highest mortality of any disease in the first and second year. All cases of bronchopneumonia must be looked on with suspicion. He had not had an experience with diphtheria. Chickenpox cannot be combated by isolation; the ward must be closed.

GERSTLEY, Chicago.

OSSEOUS AND CARTILAGINOUS METAPLASIA IN THE TONSILS IN A DIPHTHERIA CARRIER. CAESER HIRSCH and M. H. CORTEN, Ztschr. f. Hals-, Nasen- u. Ohrenh. **19**:397 (Dec. 22) 1927.

A case of osseous and cartilaginous metaplasia in the tonsils of a diphtheria carrier is described. The tonsils were examined histologically after removal. Bone was substituted for young cartilage developing from connective tissue. The bone continued to grow within certain limits. Inflammatory changes were not found in the connective tissue. Diphtheria is a typical disease of the surface which never penetrates deeper by filtration. Degenerative processes beneath the surface could be expected, in consequence of the resorption of toxins. These processes were not found. Yet, they may have existed previously and caused atrophy of the adenoid tissue in the tonsil. Larger scars, in diphtheria, are usually signs of a mixed infection. The capsule of the tonsil is favorable to the formation of cartilage with secondary ossification, because it develops from the second pharyngeal pouch. The formation of cartilage and bone in the author's case had continued through opposition after the inflammation had subsided. This growth persisted until the tonsils were removed. Therefore, a genuine metaplasia of the connective tissue into cartilage, with secondary endochondral and ecchondral ossification, had taken place. The diphtheria bacilli had found a favorable soil in the deep crypts of the tonsils in which they could live for an indefinite time without being injurious to the carrier. They could scarcely be influenced by disinfectants. A direct connection between the diphtheria bacilli and the metaplastic processes could no longer be shown.

AMBERG, Detroit.

DICK SKIN REACTION AS A TEST OF IMMUNITY IN SCARLET FEVER. E. LORENZ and E. NOBEL, Ztschr. f. Kinderh. **44**:108 (Aug.) 1927.

The Dick toxin obtained from various sources acted differently; for example, the Wiener toxin gave more than double the number of positive reactions in comparison with the American toxin, and in the same children tests with various toxins varied 33 per cent. The cause of this variation does not depend on the type of child but on the toxin itself. Streptococci of different derivation usually act more weakly than the Dick toxin. A uniform application and a standardization of the Dick toxin is essential for successful research.

PROTECTIVE VACCINATION AGAINST DYSENTERY. H. POGORSCHELSKY, Ztschr. f. Kinderh. **44**:200 (Aug.) 1927.

According to Pogorschelsky, although his material was small, protective inoculation against dysentery as used by him is encouraging, but nothing definite can be said about the duration of the protection thus given. The infants under his care were observed for from eight to sixteen weeks, and several children remained in the hospital six months without getting dysentery. Six children became ill with dysentery in spite of vaccination.

GANGRENE IN THE COURSE OF EPIDEMIC MENINGITIS. SIEGFRIED LEVY, Ztschr. f. Kinderh. **44**:230 (Aug.) 1927.

One month after a severe case of epidemic meningitis, an asphyxia of short duration developed in the hands and feet. The asphyxia in both feet and in the left hand disappeared within a day, while in the right hand gangrene developed which appeared first as a constriction of the terminal phalanges of two fingers.

In the course of the next two weeks the terminal phalanges of the middle finger dropped off, and at the same time a slight necrosis of the thumb and of the little finger appeared. Soon, a special sensitiveness of the whole right hand to pain was observed, and in the course of the next month, that is, seven weeks after the asphyxia, a separation of the end phalanx of the index finger and a slight necrosis of the fingers not yet affected occurred. At the same time there arose in the parietal bone sharply marked necroses which affected the spongiosa and from which streptococcic pus was discharged. In the course of fourteen months, new necroses were not observed, but, on the other hand, hydrocephalic symptoms increased constantly.

EMERSON, Boston.

Chronic Infections

STRABISMUS AS A SYMPTOM IN CONGENITAL SYPHILIS. LLOYD B. DICKEY, J. A. M. A. **90**:385 (Feb. 4) 1928.

Strabismus is not usually mentioned as a symptom of congenital syphilis. In the last year 26 per cent of twenty-seven patients with late congenital syphilis had evidence of strabismus, and in two it was the complaint for which the patient visited the clinic. Because strabismus may occasionally be due to or associated with syphilis, a plea is made for a blood Wassermann test on every child suffering from strabismus.

BONAR, Salt Lake City.

ASTHMA, TRACHEOBRONCHIAL ADENOPATHY AND TUBERCULOSIS IN CHILDREN. P. NOBECOURT, Internat. Clin. **1**:127, 1928.

Nobecourt gives an analysis of personal statistics covering a period of seven years, concerning the coexistence of asthma, tracheobronchial adenopathy and tuberculosis. In 82 per cent of the cases, asthma precedes glandular symptoms by several years. The adenopathy did not precede the asthma in any of the cases. Tuberculosis is not a cause of asthma in Nobecourt's experience. When an asthmatic patient suffers from tracheobronchial adenopathy, the latter is usually nontuberculous. When asthma coexists with tracheobronchial adenopathy, one may usually discover one of the usual etiologic agents of asthma, such as infection of the upper respiratory tract and allergy.

Tracheobronchial adenopathy may cause lesions of the pneumogastric nerve. Irritation of the pneumogastric and sympathetic nerves by hypertrophied mediastinal ganglions may contribute to the state of hypervagotonia frequently observed in asthmatic persons.

MILO MILLER, South Bend, Ind.

A CASE OF JUVENILE GENERAL PARESIS. H. R. C. RUTHERFORD, Irish. J. M. Sc. **6**:49 (Feb.) 1928.

A boy, aged 10 years, was admitted to hospital in a restless and elated condition, with grandiose ideas. He had sluggish pupils and increased knee jerks on both sides. At the time of birth the boy had had a rash, which had disappeared under treatment. When the patient was 3 years old, his father had developed mental symptoms, and a diagnosis of general paralysis had been made. The Wassermann reaction with the boy's blood was found to be positive, and he was treated with mercury, arsenic and iodides. The first mental changes noted were an addiction to lying and stealing money. He told stories of extraordinary achievements. One day he knocked down a woman who failed to return his salutation. Then he passed into a state of excitement and violence. After a few weeks he became depressed, but a short time after that changed again into a stage of excitement. The cerebrospinal fluid showed 90 cells, mainly mononuclears, increased globulin, negative Lange and positive Wassermann reactions.

PETERSEN, Montreal.

VACCINATION WITH B.C.G. IN ALGERIA, 1924-1927. E. SERGENT and H. ROUGEBIEF, Ann. de l'Inst. Pasteur **42**:35, 1928.

Between Nov. 4, 1924, and Dec. 1, 1927, 1,308 children were vaccinated. Of these, 564 were from 1 to 3 years of age on Dec. 1, 1927. It was possible to follow 208 of these children; 62 were constantly exposed to tuberculosis and 146 were not. Of the 208 children, 34 died during the interval, three from the exposed group and thirty-one from the supposed nonexposed group. Only one of these deaths was due to tuberculosis, and in that case diagnosis was doubtful. It occurred in the nonexposed group. In unvaccinated children it is reported by another author that from 15 to 20 per cent of the deaths occurring in children from 0 to 30 months of age are due to tuberculosis in Algeria.

M. S. MARSHALL.

GANGRENOUS STOMATITIS DUE TO BISMUTH. L. SPILLMANN and WEISS, Bull. Soc. franç. de dermat. et syph. **35**:63, 1928.

The patient, aged 17, had congenital syphilis. Following a series of injections of bismuth, she developed a severe stomatitis with serious systemic symptoms. Favorable therapeutic results were obtained from antigangrenous serum and local applications of Labbarraque's solution and neoarsphenamine. The author warns against treatment with heavy metals if the gums are in bad condition.

ARCH. DERM.

CONGENITAL CERERospinal SYPHILIS. A. GAREISO, Rev. méd. latino-Am. **13**:429 (Dec.) 1927.

The patient was a child, aged 8, who died in dementia. The clinical diagnosis was juvenile paralysis. The symptoms were spastic paraplegia, spastic paralysis of the right arm and paralysis of the facial nerve of the same side. The test of the cerebrospinal fluid gave a positive reaction. The author considers the differential diagnosis with multiple sclerosis, Strümpell familial paraplegia and medullary tumors.

PARDO-CASTELLO, Havana.

LATENT COLD HEMOGLOBINURIA IN CONGENITAL SYPHILITIC CHILDREN. LEO STEINBOCH, Monatschr. f. Kinderh. **38**:336, 1928.

Cold hemoglobinuria is a syndrome in which after exposure to the cold the patient feels general malaise, nausea, pallor and cyanosis of the extremities, pain in the back and often chills and fever and on coming into a warmer temperature, passes a blood colored urine. The color is due to hemoglobin. The studies of Donath and Landsteiner have shown that this is due to a specific antibody found in the blood of these patients and activated by the cold. The writer was interested in the number of syphilitic children who might harbor such an antibody. Of thirty-three patients with congenital syphilis, three or 9 per cent, harbored this specific hemolysin. These were aged 12, 15 and 18 years, respectively.

CIRCUMCISION-TUBERCULOSIS OF FIVE YEARS' STANDING. FEDERE, Monatschr. f. Kinderh. **38**:537, 1928.

Up to 1921, fifty-eight cases have been reported, in twenty-one of which the patients were living at the end of the first year. The writer reports a case in an infant, age 1 month, followed for five years and ending in recovery.

GERSTLEY, Chicago.

A REPORT OF THREE YEARS OF THE SYPHILIS CAMPAIGN OF THE WELFARE STATION FOR MOTHER AND CHILD. JAN ZIENKIEWZ, in Vilna, Opieka Nad Dzieckiem (Polish) **6**:108, 1928.

In April, 1924, the children's clinic of the city of Vilna, through the opening of its own ambulatorium for syphilitic children, gave rise to the organization of the

campaign against syphilis in childhood. After two years this ambulatorium was placed in a welfare station for mother and child, which undertook the investigation of the families and homes of the registered patients. Of 178 syphilitic children up to 15 years of age, who had entered the station previous to April 1, 1927, 21.9 per cent died. Of the number of new-born and infants (121), 31.2 per cent died. Of those altogether untreated, there were 90.9 per cent. Of those insufficiently treated, (brought irregularly), there were 66 per cent. Of those systematically treated, there were 7.2 per cent. The combined treatment with neoarsphenamine was used. In the presence of eruptions on the skin in infancy, satisfactory results were obtained through the use of stovarsol by mouth. AUTHOR'S SUMMARY.

Internal Diseases

HEREDITY IN HEMOPHILIA. MADGE THURLOW MACKLIN, Am. J. M. Sc. **175:** 218 (Feb.) 1928.

Dr. Macklin shows that the offspring of a man affected with hemophilia will not have this disease provided the man marries a normal woman who is not a carrier. The sons of such a man will not only be normal themselves but they will not be able to transmit the defect to their descendants. The daughters of such a man will be outwardly normal, but they will all be carriers of the disease, and likely to pass it on to 50 per cent of their sons. Fifty per cent of the daughters of a woman who is a carrier of hemophilia are likely to be carriers themselves. The only persons in a hemophilic family who can marry with impunity are the unaffected males and their descendants. All daughters of hemophilic males are carriers and should not reproduce.

Hemophilia is a disease so tragic in effect that it is essential for those who bear the taint in the family to know the possibilities of passing it on.

HENSKE, Omaha.

CONGENITAL CANCER: CASE REPORT. EVERETT L. LAIN, M. J. & Rec. **127:** 377, 1928.

The foregoing case was reported in a girl, aged 9 months. A few hours after birth a small tumor was noticed in the left supraclavicular region by the physician, who suggested the presence of a cervical rib. When the child was 6 months of age, the mother noticed that the tumor was growing, and the physician then suggested that there was an enlarged lymph gland. The tumor continued to grow and became slightly tender and a deep bluish red until the child was 9 months old, when she was examined by Dr. Lain. At this time the overlying skin was broken with irregular, proliferating, granulomatous-like tissue from which exuded seropurulent matter intermixed with blood. Dulness was present over the upper part of the left side of the chest. The child was sent into the hospital for complete laboratory tests including biopsy. The biopsy examination was made by Dr. Louis A. Turkey, who made the diagnosis of carcinoma derived from embryonic ectoderma. The report of examination is given in full in the paper. A radical operation was refused by the parents, and the child was treated with radium, after which the parents took her home. A month later the child returned with a marked reduction in the size of the original tumor, but was suffering from a dry hacking cough and cachexia, and other plainly obvious evidences of metastasis. X-ray examination at the time revealed an almost complete filling of the upper part of the left side of the chest with neoplastic growths as well as a beginning invasion of the right side of the chest with the same tumor mass. The patient received one palliative x-ray treatment and was then taken home. Two weeks later, she died of carcinomatosis.

WILLIAMSON, New Orleans.

THYMUS DEATH IN A CHILD. HERBERT L. COE and B. E. PEDEN, Northwest Med. **27:**177 (April) 1928.

Coe and Peden report multiple anomalies occurring in the child of a mentally subnormal mother, whose own father was the father of the child. This child was

observed in several hospitals over a period of twenty-two months. When first seen the child showed harelip, cleft palate, transposition of all viscera and a mitral murmur. At the age of 10 months, the first operation was performed on the palate under a well tolerated ether anesthesia. Shortly after this operation, x-ray examination revealed the presence of an enlarged thymus. A second operation at 13 months and a third and fourth soon afterward were done under ether, which was also well tolerated. At the age of 22 months, a fifth attempt was again made to produce ether anesthesia in which the child died. Autopsy showed the following anomalous conditions: harelip; cleft palate; threadlike adhesions of the lungs to the wall of the chest; hypertrophied heart in the right side of the chest, with patent interventricular septum, and narrowing of the great vessels; enlarged thymus, weighing 45 Gm., which flattened the trachea beneath it; the liver on the left side; the pylorus pointing to the left; the spleen on the right side and the cecum in the left iliac fossa.

This case is of interest because the child survived the production of ether anesthesia four times, but died during the fifth.

THE THYMUS IN CHILDHOOD. BARNET E. BONAR, Northwest Med. **27**:178 (April) 1928.

Bonar reviews the anatomy, physiology and diseases of the thymus. Enlargement of the thymus, its symptoms, physical signs and treatment are discussed in some detail.

HYPERTROPHIC PYLORIC STENOSIS OCCURRING IN PREMATURE TWINS. J. B. BILDERBACK, Northwest Med. **27**:182 (April) 1928.

Bilderback reports stenosis in premature twins. The first infant, who weighed 4 pounds and 4 ounces (1,927.7 Gm.), developed symptoms at the age of 21 days, was operated on at 30 days and died at 38 days. The second child, who weighed 4 pounds (1,814.3 Gm.) at birth, developed symptoms at 30 days, was operated on at 40 days and made a complete recovery.

Bilderback quotes Keilman as stating that stenosis may be present without symptoms. Bilderback believes that the symptoms defer their appearance until the onset of spasm. Symptoms have been noticed as early as fourteen hours after birth and may not appear for six or eight weeks.

EXAMINATION OF OVER 3,000 CHILDREN FOR HEART DISEASE. T. HOMER COFFEN and HELEN A. CAREY, Northwest Med. **27**:185 (April) 1928.

While competing in an annual spring track meet, a number of pupils in the grammar grades collapsed during the exertion. This led to careful examination of all entrants to the meet. Murmurs were present in 191 persons, in ninety-two of which they did not appear until after exercise. Of the 191, fifteen were found to have chronic rheumatic heart disease. Murmurs at the base, usually systolic, were frequent and often were associated with good tolerance of exercise.

SCOTT, Philadelphia.

DIARRHEA AND ENTERITIS IN PORTO RICO. E. B. PHELPS and J. V. DÁVILA, Porto Rico Rev. Pub. Health **3**:468 (May) 1928.

This is the second article of the series and deals with the water supply. The authors are of the opinion that these diseases may be reduced by improvement of the water supply. They also conclude that in infants under 1 year of age diarrhea and enteritis are of a somewhat different origin and possibly of a somewhat different type from that affecting the higher age group. In all probability the disease reported in infants over 1 year of age is to a large extent water borne.

SANFORD, Chicago.

ANGINA PECTORIS IN CHILDREN. E. J. STOLKIND, Brit. J. Child. Dis. **25**:1 (Jan.-March) 1928.

The author describes four cases of his own of angina pectoris in children ranging from 9 to 14 years of age and lists twenty-five additional cases recorded by other observers. He believes that the pathogenesis of angina pectoris is of complex character, its main factors being (1) the chemical and "toxic" substances circulating in the blood; (2) the state of the nervous system, especially the autonomic system, and the disposition of the patient and (3) the condition of the heart and the aorta.

Angina pectoris is rare in children, and in those who have asthma and who complain of oppression and constriction the condition should not be mistaken for it. Likewise, patients with extrasystoles may show symptoms similar to those of angina pectoris, such as fear, pain, etc. The severe pain in the region of the heart which radiates to the left shoulder and sometimes to the right is the most characteristic symptom. The more the heart and the aorta are affected the graver is the prognosis as to life. Under treatment, various drugs, including digitalis, morphine and nitroglycerine, are mentioned, as well as surgical measures, such as section of the sympathetic nerve, though the latter is still in the experimental stage.

SUBACUTE INFECTIVE ENDOCARDITIS IN CHILDHOOD. BERNARD SCHLESINGER, Brit. J. Child. Dis. **25**:33 (Jan.-March) 1928.

Included under the term subacute infective endocarditis are those cases which after a prolonged subacute course of intermittent fever and progressive toxemia almost invariably end in death. The author admits, however, that rheumatic heart disease is also most certainly "infective."

Both congenital malformations of the heart and previous attacks of rheumatic endocarditis favor the incidence of this disease. In this series of fourteen cases, six patients had previous attacks of rheumatism and two showed congenital malformations.

The disease is rare in children; during sixty-five years there were only ten cases at the Hospital for Sick Children, Great Ormond Street, as compared with 341 cases of rheumatic endocarditis. The bacterial evidence in this study is not complete.

Splenic enlargement, petechiae and clubbing of the fingers are mentioned as prominent signs in this disease. An enlarged spleen is much more common than in the rheumatic patients, and at autopsy infarction was invariably found whereas the rheumatic patients show a large friable "septic" spleen and infarction only on rare occasions.

Acute nonsuppurative pericarditis is an uncommon complication of subacute infective endocarditis, though at autopsy one frequently finds evidence of an old rheumatic pericarditis in these cases.

A CASE OF ACHALASIA OF THE CARDIA IN A CHILD OF SEVEN YEARS. W. GORDON SEARS, Brit. J. Child. Dis. **25**:48 (Jan.-March) 1928.

Achalasia of the cardia is synonymous with "cardiospasm." A boy, aged 7 years, was treated with saline and dextrose solutions by rectum for two days and then a Hurst's achalasia "mercury bougie," size 24, was passed and left in position for fifteen minutes. This was repeated four hours later. Thereafter, the bougie was passed three times a day, this being gradually decreased to once a day; the patient was discharged at the end of seven weeks. Vomiting did not occur except the first day that the bougie was passed. About nine weeks after discharge, the symptoms of cardiospasm recurred and the boy was readmitted to the hospital for a few days. He had tired of having the tube passed and a recurrence of the symptoms was the result.

Unfortunately, the author does not state what the ultimate prognosis of this form of treatment is.

LANGMANN, New York.

ENDOCARDITIS AND CONGENITAL HEART DISEASE. A. B. MARFAN, Nourrisson **15**:329 (Nov.) 1927.

A foundling came under observation at the age of 8 days. After a few days in the hospital, she was considered normal and was sent to a convalescent home in the country. At the age of 6 weeks she was returned on account of a gastro-intestinal disturbance. It was then noted for the first time that the heart seemed enlarged and presented a loud systolic murmur, which was audible all over the precordium but was loudest in the third intercostal space to the left of the sternum. The infant appeared anemic but lacked cyanosis. The liver and spleen were normal. Death ended an illness of several weeks. During this time the cardiac murmur disappeared, and signs of infection of the lung appeared; fever was not conspicuous and was interrupted by long periods of apyrexia. Symptoms of congenital syphilis were not present.

Autopsy revealed a three chambered heart due to an absence of the inter-auricular septum; there was also a small semilunar defect in the interventricular septum; the pulmonary artery was dilated and the aorta small; the ductus arteriosus was obliterated; a vegetative endocarditis covered the mitral and tricuspid valves. Neither smears nor sections revealed any micro-organisms; so the etiology remains obscure, though the author suggests the possibility of a syphilosis. Attention is also directed to the frequent association of endocarditis and congenital malformations of the heart.

PYELITIS. P. LEREBOULLET and F. SAINT-GIRONS, Nourrisson **15**:336 (Nov.) 1927.

The remarkable feature about the case of pyelitis reported was the exhibition of a series of attacks of coma. The illness was ushered in by a gastro-intestinal upset which was followed by the presence of albumin in the urine. The first attack of coma was considered uremic, but chemical analyses of the blood showed a normal blood urea at this time and subsequently. Several other attacks of coma followed at intervals of a few days. Some were accompanied by fever, and one was so severe that it was followed by a toxic amblyopia. Ureteral catheterization gave urine containing many leukocytes and gram-negative bacilli, which cultures showed were colon bacilli. An autogenous vaccine was prepared, and injections were made in increasing doses. The attacks of coma continued with decreasing frequency and intensity. Finally, a bacteriophage was prepared and administered by mouth. Complete recovery ensued.

McCLELLAND, Cleveland.

A CASE OF HYPOPLASTIC ACHONDROPLASIA. A. LOFFREDO, Pediatria **36**:481 (May 1) 1928.

A case herein reported is a typical one of achondroplasia. The little girl lived twenty-two days. Clinically, enlargement of the liver and spleen was present, but the Wassermann reaction was negative. At autopsy, besides the usual condition reported extensively in the literature, there was in this case a generalized sclerosis of the glands of internal secretion, which the author considers of hereditary syphilitic origin. Syphilis is therefore advanced by Loffredo as an important etiologic factor in this condition, perhaps the most frequent, though certainly not the only one. The author thinks that in this case the arrested development was due to the polyglandular sclerosis caused by hereditary syphilis.

A CASE OF CHLOROMA. P. PERAZZI, Pediatria **36**:486, 1927.

A boy, aged 3½ years, was brought to the hospital four months after his oldest sister had first noted an enlargement of the head. At the time of examination, the child was pale and undernourished. The head was enlarged in all diameters, and through the hair could be seen a rich network of angiectatic vessels, which gave the scalp a cyanotic appearance. A large swelling in the left parietal region and exophthalmos on that side were present.

Both Wassermann and tuberculin reactions were negative. Nothing in the family history pointed to these diseases. There was a history of slight trauma to the scalp and head at 2 years of age.

Examination of the blood was as follows: red blood cells, 3,200,000; white blood cells, 14,000; hemoglobin content, 55 per cent; polymorphonuclear neutrophils, 82 per cent; eosinophils, 4 per cent; lymphocytes, 6 per cent; monocytes, 3 per cent; neutrophilic myelocytes, 1 per cent; metamyelocytes, 2 per cent. Anisocytosis and poikilocytosis of the red cells were present, and normoblasts were numerous.

A piece was removed from the cranial tumor, fixed in alcohol and stained by the Giemsa method. Examination then disclosed an adenoid network, which at times was thin; it contained nests in which hematocytoblasts, myeloblasts, promyelocytes, neutrophilic, eosinophilic and basophilic myelocytes, and a few neutrophilic polynuclears and lymphocytes could be seen. There were, moreover, several normoblasts often with pyknotic nuclei. Frequent small hemorrhages were present in the parenchyma.

The histologic diagnosis was myeloid chloroma.

The child died twenty-two days after admission. The case is interesting because myeloid chloroma is not nearly as frequent in childhood as the lymphatic variety, and because the diagnosis could be reached only by biopsy.

SALA, New York.

INVESTIGATION ON THE INFLUENCE OF DEXTROSE AND INSULIN ON THE ACETONE AND β-OXYBUTYRIC ACID CONTENT OF BLOOD AND URINE IN DIABETES MELLITUS. O. PUCSKO, Wien. Arch. f. inn. Med. **15**:331, 1928.

The influence on the ketone level of the blood of the combination dextrose-insulin and insulin-dextrose given in various combinations and time intervals was investigated. The ketone bodies excreted in the urine were determined at the same time.

Uninfluenced by various therapeutic procedures, the ketone bodies of the blood show considerable variation during various intervals of a twenty-four hour period. The combination dextrose-insulin influences the ketonemia more favorably than the combination insulin-dextrose. The most favorable influence is produced by giving dextrose first intravenously and one and one-half hours later insulin subcutaneously.

There is considerable nocturnal excretion of ketone bodies in the urine, regardless of the conditions of the experiment. The combination of dextrose-insulin, with the dextrose given first and the insulin one and one-half hour later, seems to offer the best therapeutic possibilities in the treatment for diabetes mellitus.

SCHLUTZ, Minneapolis.

CONTRIBUTION TO THE KNOWLEDGE OF POLYCYTHEMIA IN CHILDHOOD. CLINICAL RESEARCHES AND HEMATOLOGIC STUDIES. A. HOTTINGER, Ztschr. f. Kinderh. **44**:61 (Aug.) 1927.

Up to the present there have not been any systematic studies of the blood and the metabolism of children with polycythemia, but cases taken from the literature may be grouped readily into two classes, clinical and hematologic.

1. The clinical cases are those of purely idiopathic heredofamilial type, with onset in the first years of life. As a result of the polycythemia there gradually develops cyanosis, signs of stagnation of the circulation, clubbing of the fingers and a general hypoplasia of the body, expressed especially in early limitation of growth and length.

2. The hematologic cases are those of an isolated and symptomatic type occurring in various dystrophic conditions in children. They are: (*a*) gianʻism and obesity with polycythemia beginning in the first years of life; (*b*) normal growth in length and the eunuch type of dystrophia adiposogenitalis with polycythemia beginning in puberty; (*c*) dwarfism and obesity with polycythemia beginning in prepuberty.

It seems important to the investigator that genuine polycythemia may occur as one of the signs of a symptom-complex based on endocrine pathologic changes.

Results of the hematologic studies showed a real plethora dependent in the familial form on the increase of the absolute number of erythrocytes with diminution of the total plasma. In a case of symptomatic polycythemia with dystrophia adiposogenitalis, there likewise occurred a real increase in the absolute number of erythrocytes and the amount of plasma. The studies also showed an increased amount of albumin in the serum of the familial form and a normal amount in the sporadic form; an increased amount of blood creatine with diminished urea and creatinine; an extremely slowed speed of precipitation of the red corpuscles and abnormal coagulation and mild eosinophilia. Normal values were obtained for the carbon dioxide combining power of the hemoglobin, the carbonic acid content of the plasma, resistance to hypotonic salt solution and isotonic solutions of saponin, for the blood sugar, cholesterin, residual nitrogen and serum salts. The basal metabolic rate was increased in all cases. Functional tests of the liver and suprarenals were normal. There was a normal lowering of the blood sugar with epinephrine hydrochloride and a mildly positive alimentary hemoclasis.

PERITONITIS IN INFANTS. ELISABETH VON SCHOPF MAYER, Ztschr. f. Kinderh. **44**:100 (Aug.) 1927.

According to the observations of Elisabeth von Schopf Mayer, it seems to be established that the disposition of the peritoneum in infants, especially premature infants, to metastatic, septic infections is relatively high. She is convinced that infections do not migrate from the intestinal mucosa, however, judging from the eight cases which she has reported with autopsy. In only one case was an acute infection without formation of ulcers found in the intestinal mucous membrane, and here an infection of the peritoneum directly from the intestine is not inconceivable. For all the cases, in her opinion, the path of infection is through the blood or the lymph stream, especially from the nose. In favor of this assumption is to be noted, in the first place, the septic feature of the disease picture in its course, as well as the disappearance of severe dyspeptic symptoms. The fact that the greater number of her cases of peritonitis occurred in premature children does not need, in the light of the exhaustive researches of Ylppö, a detailed explanation and only strengthens the impression that, in relation to constitution, premature infants show a distinct inferiority. A definite disposition of the peritoneum to infection exists in them and can be ruled out only by a consideration of all the evidence.

PROPHYLAXIS AGAINST GOITER IN INFANTS AND CHILDREN. E. MAURER, Ztschr. f. Kinderh. **44**:114 (Aug.) 1927.

By the feeding of iodized milk, according to researches at the Agricultural Chemical Institute at Weihenstephan, by long continued addition of moderate amounts of potassium iodide to the food of cows and of goats, the iodine content of milk could be raised in consistent measure, and the use of such milk was well borne by infants. One hundred and eighty milligrams of iodide was fed to a goat daily for four weeks and 76.45 mg. of iodide to a cow for the same length of time.

THE ADDITION OF IODINE TO MILK AND PROPHYLAXIS AGAINST GOITER. K. SCHARRER, Ztschr. f. Kinderh. **44**:124 (Aug.) 1927.

By the addition of iodine to the food of milk producing animals, especially cows, an amount of iodine from the milk could be obtained which, with respect to its constancy and the absolute height of the iodine curve for milk, did not go with a single exception beyond the limits of the physiologic and safe dosage of iodine. A dosage of 76.45 mg. of iodine in the fodder increased the iodine in the milk to ten times the normal amount.

EMERSON, Boston.

DIABETES MELLITUS IN CHILDREN. KARIN WILNÄS, Acta Paediat. **8:** supplemen 1, page 1 (June) 1928.

The entire supplementary number is devoted to the single study of seventeen patients, of whom three were definitely nondiabetic and in one of whom the condition was doubtful (exophthalmic goiter). While individual case reports are faithfully and well presented, the author is prone to draw conclusions scarcely warranted by the size of the study. Moreover, certain instances of treatment and response, which occurred in the early insulin period when this therapeutic agent was not at all times available in the desired amounts, form a difficult basis of comparison with modern practice; and the pace of investigation along these lines has been so rapid that the author's review of literature and interpretation of results suffer at times from his failure to include the most recent observations, particularly of American work. A single policy of therapy was not consistently followed, for the study was commenced in the early insulin period and continued up to the current year, during which interval almost every clinic has undergone modification of its concept of the treatment for diabetes.

As regards special studies in the response of diabetic and nondiabetic persons to alimentary administration separately of water, dextrose, starch, protein and fat, and in a few instances of mixed meals, the author contributes valuable observations. At frequent intervals, she studied the blood content of water, sugar and acetone bodies, and the urine with observations of volume and qualitative tests for reducing substances, acetone and oxybutyric acid. New discoveries were not made, but the results of other investigators are corroborated. In the transition from the sugar-free to the glycosuric state, the first urinary change is a diuresis; then, sugar appears and then a diminution in diuresis with an increase of sugar concentration in the urine excreted occurs.

The effect of intercurrent infections depends to some extent on the condition of the patient at the time, partly also on the nature of the infection. If the patient is doing well, an infection may have little if any effect, and this will be of transitory nature. Simple diarrhea even exerts a beneficial influence sometimes. On the other hand, if the patient is doing poorly, an infection may produce profound deleterious effects. The particular infections which have the most harmful influence are those of pyogenic type or those giving rise to polymorphonuclear leukocytosis, such as localized superficial infections, pharyngitis, otitis and pneumonia.

In general, tolerance and the patient's sense of well being are augmented in summer, but are in jeopardy at other times of the year.

The article is in French and contains a bibliography of 363 references.

McINTOSH, Baltimore.

Nervous Diseases

PNEUMOCEPHALUS OF BACTERIAL ORIGIN. W. E. DANDY, Arch. Surg. **15:**913 (Dec.) 1927.

This interesting case of pneumocephalus occurred in a boy, aged 6 years, following a mastoid operation. About three weeks after the operation, the clinical signs indicated the possibility of an abscess of the temporal lobe. Exploration revealed an abscess which was tapped, but symptoms of increased intracranial tension returned and tapping was done about every two days, until finally a permanent drain was put in for five days. A roentgen-ray examination revealed a large air shadow in the temporal lobe, and when the abscess was tapped bubbles of air escaped through the needle. Cultures of the puss revealed a gram-negative bacillus, which produced gas in dextrose and maltose, was nonmotile and nonspore-bearing and which did not grow aerobically. A brief report of two cases in the literature due to *B. welchii* is added.

N. ENZER.

FAMILIAL MONGOLIAN IDIOCY. MAXWELL P. BOROVSKY, J. A. M. A. **90**:459 (Feb. 11) 1928.

Multiple cases of mongolism in one family are relatively rare. In this report, three female mongols were observed as the offspring of two sisters. The father of one of these families had five normal children by a first wife. This observation speaks for a familial endogenous maldevelopment as the etiologic basis in this obscure condition.

UNILATERAL SYMPTOMS IN MENINGITIS. ABRAHAM LEVINSON, J. A. M. A. **90**:520 (Feb. 18) 1928.

When unilateral neurologic symptoms occur, one is often inclined to rule out the presence of meningitis and to think of abscess of the brain, tumor of the brain, encephalitis or poliomyelitis. The unilateral symptoms may be intermittent or constant, may occur early or late in the disease and may be found in either a primary or a secondary meningitis caused by any bacteria. At autopsy, unilateral or localized pathologic change may or may not be found. Examination of the cerebrospinal fluid is the best means of differentiating meningitis with unilateral symptoms from other conditions.

PARALYSIS OF THE RIGHT DIAPHRAGM ASSOCIATED WITH BRACHIAL PALSY. MENDEL ZELIGS, J. A. M. A. **90**:762 (March 10) 1928.

A case of paralysis of the right side of the diaphragm is reported associated with brachial paralysis. The author found few cases reported of this association and, because of the close anatomic relationship between the phrenic nerve and the brachial plexus, believes that more such cases would be diagnosed if a fluoroscopic examination of the chest is made in every child with brachial palsy.

BONAR, Salt Lake City.

ANOREXIA NERVOSA: HYPOGLYCEMIA OR HYPO-ADRENIA? C. S. LEEDE, Northwest Med. **27**:233 (May) 1928.

Leede reviews a number of cases of anorexia nervosa in adults and believes that there may be an endocrine basis for the condition. Most of the patients showed hypoglycemia, low blood pressure and a low basal metabolic rate. Improvement followed rest, the administration of thyroid extract and the feeding of dextrose. Leede quotes three cases of complete or almost complete pyloric obstruction with normal blood sugars to show that the hypoglycemia is not due to the starvation. He believes that many of the cases are in reality suprarenal hypofunction and that the hypoglycemia and hypofunction of the thyroid are secondary states.

SCOTT, Philadelphia.

THE TREATMENT OF INFANTILE CEREBRAL PARALYSES. NEIL HOBHOUSE, Lancet **1**:409 (Feb. 25) 1928.

Certain features may be indicated which place a case of infantile cerebral paralysis beyond the reach of effective treatment. These features are: evidence that the disease is progressive, presence of a profound degree of mental defect and persistent occurrence of fits. Cases in which there are choreiform or athetoid movements and cases in which a high degree of muscular rigidity is present, sufficient to make active movement impossible, are unfavorable, though an attempt at treatment should be made. In cases with such marked rigidity, nothing can be done unless the spasm can be reduced by surgical means. Excluding these, there remains a large number of cases in which the prognosis is not so gloomy. It is of greatest importance, however, that treatment be started within the first two years.

The question arises as to whether spastic paralysis may be averted in an infant whose condition at birth suggests intracranial hemorrhage. Opinion is divided

on the merits and demerits of lumbar puncture in such a condition; usually, it is disappointing, and the disturbance of the operation involves an element of danger. The safest prophylactic routine is to keep the infant at complete rest and feed it from a medicine dropper, so as to obviate the effort of sucking.

No form of passive treatment seems to be of avail in preventing the onset of spasm and contracture, whereas some forms aggravate it. Active movements seem to produce an effect on the tone and functional activity of the affected limbs. The possibility that new synaptic connections may be formed, that other neurons may acquire the functions which the as yet undeveloped pyramidal tracts were intended to subserve is entirely hypothetic; yet it is suggested by the remarkable recovery of function in the child as compared with the adult. Relative integrity of the cortical areas may be necessary for improvement; in imbecile children active movement has been found to aggravate spasm. In the earlier months of life, while behavior is still to some extent controlled by the infracortical centers, and if the child can be assisted to make habitual use of the affected muscles, contracture does not usually develop, and results of treatment are often remarkably satisfactory.

Warm baths may produce some degree of relaxation; massage and passive movements are ineffective but innocuous; electrical stimulation is harmful and contraindicted. To promote active movement the child should be placed in a sitting posture as soon as possible. In many cases, this may be done by propping it up with pillows; in other cases, the child may be placed in a baby's chair with a pillow between its abdomen and the rung or crossbar of the chair. Similar efforts should be made in overcoming the retardation in crawling and standing. In hemiplegic cases, the sound arm should be strapped to the side about half the day in order that the child may use the weak one. Any activity favoring the use of both arms should be instituted, such as wheeling a loaded wheelbarrow without spilling the contents. To facilitate walking, the following aids should be used: a wheeled frame with crutch supports adjusted to the axillae, the handle bar of a doll's perambulator in the front of which weights are placed, or a horse tricycle; the last is particularly useful in cases with adductor spasm. If the range of passive movement is restricted by contractures, surgical interference is necessary before active movements will do any good. Supination is especially difficult to establish, and some measure, such as a Stoffel operation, may be necessary to overcome the pronator spasm. The author's limited experience with ramisection of the sympathetic nerve has not led him to believe that it is justifiable.

PETERSEN, Montreal.

SEROUS MENINGITIS. GEORGE T. BOYER, Canad. M. A. J. **18**:546, 1928.

The author differentiates between meningism and serous meningitis. In the former there are signs of increased cerebrospinal pressure, but the fluid is otherwise normal. In the latter the signs and symptoms are those of meningitis, the cerebrospinal fluid being under pressure and showing an increase in globulin and in cells but being culturally sterile. Twenty-four cases are analyzed. The analysis showed that practically all accompanied infections of the upper respiratory tract. Six patients died from otitis media and complications. The highest cell count in the spinal fluid was 7,000 per cubic millimeter and the lowest, 11 per cubic millimeter. Lymphocytes predominated in 70.6 per cent.

MOORE, Omaha.

VAGOTONIA. HENRY LEMAIRE, Nourrisson **15**:345 (Nov.) 1927.

During the first week of life the vagus nerve remains inexcitable, but by the second or third week the oculocardiac reflex becomes positive and remains so during the rest of infancy. The author describes the following morbid conditions in infants which he believes are due to a disturbance of the sympathetic nervous system: syncopal attacks, angioneurotic edema, Raynaud's disease, erythromelalgia (Wier Mitchell) and acrodynia. These are considered seriatim, and illustrative cases are cited. Acrodynia, the etiology of which is unknown, is included though others believe it due to a lesion of the mesencephalon.

HYDROCEPHALUS. A. B. MARFAN, Nourrisson **16**:12 and 65 (Jan. & March) 1928.

Internal hydrocephalus may be either congenital or acquired, and if acquired the condition may be acute, subacute or chronic. The acute and subacute varieties are associated with or follow some form of meningitis; the etiology of the chronic type is more subtle and varied; the distended ventricles may contain more than 500 cc. of cerebrospinal fluid; the choroid plexuses in recent cases show only inflammatory changes. Lesions of the meninges and of the aqueduct vary with the individual case. Here the author reviews the work of Dandy and Blackfan, emphasizing the differentiation between the obstructive and communicating forms of hydrocephalus. In choosing a dye for injection into the ventricles, Marfan prefers to use a 1 : 300 solution of methylene blue. Ventriculography is condemned as being too dangerous, as is also the proposal to take ventriculograms after the injection of iodized oil 40 per cent.

Congenital hydrocephalus is of two varieties: one associated with congenital malformations of the central nervous system and the other subsequent to intrauterine inflammations of the meninges or ependymas, especially when due to syphilis. Attention is also directed to those cases developing after surgical intervention in persons with spina bifida. Ill advised operations are to be deprecated.

In the treatment for hydrocephalus, reference is made to the researches of Weed and MacKibben on the effects of intravenous injections of hypertonic solutions and medication with diuretin, as described by Marriott. The attempts to effect cures by the radical surgical procedures proposed by Dandy are mentioned. These at present are fraught with too much danger to be recommended.

McCLELLAND, Cleveland.

ESSENTIAL NARCOLEPSY AND SYMPTOMATIC NARCOLEPSY OR LETHARGY. G. R. LAFORA, Arch. de neurobiol. **7**:49 (March-April) 1927.

Two cases of genuine narcolepsy and a rare case of symptomatic narcolepsy of unknown origin are described.

Case 1 was that of a man, aged 35, who suffered from frequent attacks lasting sometimes one or two hours. On some occasions, especially during periods of emotion, the patient felt sudden debility in the legs, an important symptom of true narcolepsy. Nothing abnormal was found in the somatic nervous system. The blood showed increase in lymphocytes and neutrophilic polymorphic cells. The urine showed excess of purin bases and no skatoxyl. The Wassermann test was negative, and there were no signs of congenital syphilis, although the patient was the son of a syphilitic father.

Case 2 was that of a boy, aged 13, the son of an alcoholic father, who suffered from sudden dizzy spells, which were followed by sleep. Tendency to sleep was present as soon as the patient sat down, and in some cases he fell asleep while standing. Before laughing or crying, he felt debility in the legs, followed by a dizzy spell and sleep. Antiepileptic treatment with phenobarbital and bromides did not improve the condition of the patient, but some improvement was noticed after administration of calcium chloride ad valerian U. S. P.

Case 3, that of a youth, aged 19, who was strong, tall and thin, was diagnosed at first as a case of psychic epilepsy and treated with phenobarital. After two months of marked improvement, a clinical picture of narcoleptic attacks of increased severity and length, accompanied by a few epileptic seizures and polyneuritis, presented itself. The disease developed gradually for six months, ending in the death of the patient after several days of deep lethargy with high fever and pronounced tachycardia. Autopsy was not performed. Repeated tests of urine, blood, feces and cerebrospinal fluid gave negative results; the only features in the urine, such as a reduction in the elimination of chlorides and increase in creatine, do not seem to be of enough importance to account for the polyneuritis, narcolepsy and convulsions. Analysis of the cerebrospinal fluid and other clinical data failed to

disclose the presence of a tumor of epidemic encephalitis. On the other hand, serodiagnosis and hemocultures gave negative results, as did inoculations of the cerebrospinal fluid in rabbits.

INFANTILE AMYOTONIA AND AMYOTROPHY (DISEASES OF OPPENHEIM AND WERDNIG-HOFFMANN). M. RUIZ MAYA, Arch de neurobiol. **7**:218 (Sept.-Oct.) 1927.

The article contains a discussion of the symptoms and course of Oppenheim and Werdnig-Hoffmann diseases based on observations in a case of congenital amyotonia in a child. From a comparison of this case with a case of infantile amyotrophy previously studied, the author concludes that amyotonia and amyotrophy are different syndromes rather than stages of a single disease as is claimed by some authors. Although no Wassermann test was made, the presence of a lesion of syphiloid aspect in the palms of the hands and the fact that there was improvement after mercurial medication are regarded by the author as indications of congenital syphilis; he suspects the existence of a close relation between syphilis and amyotonia in the case described.

NONIDEZ, New York.

INJURIES AT BIRTH AND THE CENTRAL NERVOUS SYSTEM. A. DOLLINGER, Ergebn. d. inn. Med. u. Kinderh. **31**:373, 1927.

The subject of this monograph of more than eighty pages, including an extensive bibliography, has important medicolegal relations, because the intracranial hemorrhages in newly born infants, due to trauma at birth, frequently arouse suspicion of infanticide. There are also judicial inquiries regarding the mental and nervous disturbances which follow such injuries. Recognition of the frequency of intracranial injury during birth is one of the remarkable developments in the knowledge of diseases of early infancy during the past decade.

Among the symptoms are convulsions, rigidity of the neck, tetany, yawning, hiccough, vomiting, anomalous sensations and body temperature, symptoms from changes in the vagus, respiratory and vasomotor nerve centers and blood in the spinal fluid. A respiratory stridor is regarded as pathognomonic. Inflammation of the injured brain tissue often occurs, both soon and long after the injury which apparently creates a place of lessened resistance. The prognosis, prophylaxis and therapy are reviewed. Early surgical intervention is advocated, in spite of the high mortality. The author believes that intracranial hemorrhage and injury at birth are responsible for many deaths officially registered under "inanition" or other designations equally indefinite.

LOUISA HEMKEN BACON.

PACHYMENINGITIS HEMORRHAGICA INTERNA. RICHARD GLAUBER, Monatschr. f. Kinderh. **38**:293, 1928.

In the course of three months, the writer saw four cases of this rare disease in the Knoepfelmacher clinic. There was no increase in the other clinics of Vienna. He discusses the causes, first considering that the condition may be due to injury of an organizing hematoma in the dura mater. He believes that injuries at birth are not so likely to be the direct causes, as the children were not new-born. In dystrophic and otherwise malnourished children, an injury to the vessels with resulting hemorrhage might follow encephalography and puncture of the fontanels. In favor of this idea, he reports a case of a large hematoma in the dura developing during scurvy.

NEUROLOGIC INVESTIGATIONS IN PREMATURE CHILDREN. W. CATEL, Monatschr. f. Kinderh. **38**:303, 1928.

In the last ten years, a number of studies on the various reflexes of the new-born have attempted to find means of diagnosing injuries received at birth by changes in these reflexes. In view of the importance of the subject, the writer records a

number of his own studies. He reopened the field by investigating the reactions in premature, new-born and older children with respect to caloric nystagmus, spontaneous nystagmus, auropalpebral reflex, eye-neck reflex and the various forms of mechanical excitibility such as the facial and peroneal phenomena.

Caloric nystagmus consists in nystagmus induced by washing the ears with 200 cc. of cold or warm water. He found cold water much more efficient than warm water. Spontaneous nystagmus was tested with the child lying on the back or on the side. The side position gives better results. The auropalpebral reflex consists in a twitching of the eyelids when the cochlear apparatus is tested with a high-pitched tuning fork. The eye-neck reflex, described by Peiper in 1926, consists of the jerking of the head backward in addition to the usual narrowing of the pupils and closing of the lids when a strong light is flashed into the eyes of a premature or young nursling.

Catel's study is complete and interesting. He discusses each set of experiments and reflexes in considerable detail. His results are important in that he finds all these reflexes extremely variable. Most of them are more frequent in the premature infant than in the mature child, suggesting the often described nervous instability of the premature infant. He does not find sufficient uniformity in the presence or absence of these reflexes to be of much clinical assistance. He goes on record in stating that the presence or absence of these reflexes will not aid in diagnosing cerebral injuries of the new-born.

PSYCHOLOGY OF CHILDHOOD. JOHANN S. GALANT, Monatschr. f. Kinderh. **39**:10, 1928.

The writer starts with the hypothesis that all that we are physically is the product of our organs of sense. He then proceeds to devote a few pages of discussion to each of the organs of sense. The article is full of quotations from older authors such as Erasmus, Darwin, Christoph Huffeländ and Jean Jacques Rousseau.

GERSTLEY, Chicago.

OBSERVATIONS ON CHOREA MINOR. ERICH GUTTMANN, Ztschr. f. d. ges. Neurol. u. Psychiat. **107**:584 (Feb.) 1927.

Although the toxic infectious nature of chorea is well known, a certain number of observers still believe that there is a certain disposition to the development of chorea. In 539 cases of chorea Wallenberg found a history of it in the parents in 2 per cent, and in relatives or offspring in 5 per cent. In 515 cases investigated by Burr, chorea was present in the family in 17.86. Guttmann was able to collect reports of chorea in families in ten cases that have been recorded in the literature. From these it seems that there is a predisposition to chorea, apart from its occurrence in connection with rheumatic fever. This disposition need not necessarily be a hereditary trait, but can be looked on as a tendency to develop chorea in soil which is prepared for it. Guttmann reports cases of chorea in which catatonia was rather a common precedent in the forbears.

ALPERS, Philadelphia.

Diseases of the Eye

THE ETIOLOGY OF LYMPHATIC KERATOCONJUNCTIVITIS IN INFANTS. G. LUPPINO, Ann. di ottal. e clin. ocul. **54**:1209 (Nov.) 1926.

The author examined the blood picture of fifty-seven patients from 2 to 14 years of age. In fifty-two a definite reduction in the red cells, with corresponding reduction in hemoglobin, was present. The white count was within the upper limits of normal, but fifty-two patients showed a relative lymphocytosis of from 28 to 38 per cent. The thirty cases showing the most marked anemia (red blood cells, 3 to 3½ million) all gave a positive Pirquet reaction. Of fourteen with moderate anemia, twelve gave positive reactions, while of eight with only slight anemia, the reaction was positive in only one, and the five with normal red counts

all gave negative reactions. Only six showed other signs warranting a diagnosis of tuberculosis, while forty-four showed other signs of lymphatism, three were scrofulous, and four were rachitic. The finding of positive Pirquet tests in from forty-three to fifty-seven cases, and the correspondence of the reaction with the degree of anemia, together with the lymphocytosis, seem to the author to indicate the presence of a tuberculous condition in most cases.

THE INFLUENCE OF DIET ON THE OCULAR DISEASES OF INFANCY. E. MORELLI, Arch. di ottal. **34**:273 (June) 1927.

The author produced pseudophlyctenules in animals sensitized to certain substances by instilling these substances later into the conjunctival sac. In animals the state of nutrition of which was lowered by injection of mercury, instillation of tuberculin produced nodules at the limbus, while in tuberculous animals, instillation of staphylococcic toxins produced true phlyctenules. Besides the diseases of xerophthalmia and hemeralopia which are definitely due to vitamin deficiency, the condition of phlyctenulosis may be produced by improper diet, which causes enteritis, with resulting absorption of toxic products from the alimentary canal. These give rise to anaphylactic phenomena of which the phlyctenule is one manifestation. This condition appears most often about the fourth year of life, when the diet is being changed. It is often possible, by means of skin tests or by observation of crises of vomiting, diarrhea or urticaria, to pick out the offending article and remove it from the diet.

GIFFORD, Omaha.

Diseases of the Ear, Nose and Throat

PARANASAL SINUS DISEASE IN INFANTS AND YOUNG CHILDREN. G. F. HARKNESS, Wisconsin M. J. **27**:112 (March) 1928.

The time and order of development of the paranasal sinuses with clinical importance are reviewed. Recurrent inflammation of the lining membranes, which prevents adequate drainage, promotes chronicity with toxic absorption. Dietetic deficiencies, especially of vitamin A, increase susceptibility to infection. Climatic conditions, especially improper humidity, of houses are productive of pathologic changes in the sinuses.

The author has seen 100 children with disease of the paranasal sinuses and notes about forty-five associated maladies of which it has been a probable causative factor though many did not show localizing subjective symptoms. The x-ray is indispensable, and transillumination is of little value in diagnosis in latent cases. Removal of diseased tonsils and adenoids results in cure in most cases. Applications that will cause shrinkage, suction and syphonage are useful. Operation is occasionally necessary.

JANNEY, Milwaukee.

MASKED MASTOIDITIS IN CHILDREN UP TO THE AGE OF TWO YEARS. F. A. MACNEIL, Canad. M. A. J. **18**:689, 1928.

In a series of forty-five patients treated by operation on the mastoid at the Children's Hospital and the Misericordia Hospital in the past two and one half years, 95 per cent were of the masked type.

Due to the anatomic peculiarities in the throat and ear of infants, they are more prone to infections of the ear and mastoid than are adults.

The local signs of mastoid disease are not the classic symptoms usually looked for but there are always definite otologic signs. The author emphasizes first, a history of infection of the ear in many but not all of the cases; second, changes of some type in the drum and third, enlargement of the periauricular glands. These signs, taken in conjunction with nutritional changes, a leukocytosis and failure to respond to local treatment and proper dietetic regimen, are sufficient to warrant a mastoidectomy.

Sixteen of the patients had both ears involved. Two cases ended fatally. There was practically no shock attendant on the operation.

MOORE, Omaha.

Diseases of the Skin

WOOD'S GLASS AND THE DETECTION OF RINGWORM BY ITS FLUORESCENT PROPERTIES. N. GRAY HILL, Brit. J. Child. Dis. **25**:54 (Jan.-March) 1928.

A small piece of Wood's glass (which contains oxide of nickel is fixed in front of a window of a Kromayer lamp, the only disadvantage of this lamp being that it is water cooled. The lamp is held 2 or 3 inches (5 or 7.6 cm.) from the scalp (the room being slightly darkened). The hairs infected with *Tricophyton microsporon* will light up as they come under the rays of the lamp and become a vivid green, the uninfected hairs being only just illuminated by the purple light. Petrolatum, brilliantine and ointments with a petrolatum base also fluoresce, but the color they give is an electric blue.

Tricophyton microsporon was the only type investigated. From twenty-five to thirty boys and about half that number of girls can be examined in an hour.

LANGMANN, New York.

NOTE ON TWO CASES OF ICHTHYOSIS BULLOSA. J. M. H. MACLEOD, Brit. J. Dermat. **40**:51 (Feb.) 1928.

Two cases are described, one in a boy, aged 9 months, and the other a girl, aged 6 years; both presented a harsh, dry, keratotic skin associated with bullae. Eight photographs showing points brought out accompany the article. Brief reference is made to cases in the literature, in which the rare occurrence of bullae in connection with ichthyosis is mentioned. In the cases here reported, the occurrence of many of the bullae so definitely in situations exposed to pressure or friction suggested that they were due to traumatism, and the flaccid character of the lesions seemed to indicate a relationship with epidermolysis bullosa.

CONGENITAL KERATOSES WITH BULLAE. W. N. GOLDSMITH, Brit. J. Dermat. **40**:59 (Feb.) 1928.

A case is reported in a boy, aged 7½ years, who presented congenital keratoses in association with bullae. The author raises the following interesting questions in his case: 1. Are the blisters traumatic, infective, dyshidrotic or pemphigoid? 2. If infective, is it external in origin or blood borne? 3. What is their relation with the fever? 4. What is their connection with the ichthyosiform erythrodermia? The literature bearing on the subject is reviewed, with review of case reports, before the question is discussed. In the case described, the congenital ichthyosiform erythroderma was accompanied by a persistent streptococcal impetigo and fever of unknown origin.

WIEN, Chicago.

CASE OF ULCERATIVE COLITIS, IN A CHILD, ASSOCIATED WITH A BULLOUS SKIN ERUPTION. W. P. WARNER, Canad. M. A. J. **18**:571, 1928.

Ulcerative colitis began in a child, aged 7 years, with profound constitutional symptoms and lasted four years with fatal termination. The recurring crops of blebs on the skin and on the mucous membrane of the nose, throat and mouth were accompanied by an aggravation of the existing diarrhea, a sharp rise in temperature and an increase in the general constitutional symptoms. An etiologic factor was not found.

MOORE, Omaha.

SKIN REACTIONS WITH HELMINTH PRODUCTS. F. K. CIESZYNSKI, Monatschr. f. Kinderh. **39**:64, 1928.

The writer attempted to diagnose the presence of worms by means of skin tests, using extracts of the worms as the agent. She found the extracts irritating to the skin, but they were not specific in their reactions.

GERSTLEY, Chicago.

Surgery and Orthopedics

USE OF FASTING DONORS IN BLOOD TRANSFUSIONS: A PRELIMINARY REPORT. WALTER V. BRAM, A. H. ZEILER and ROY W. HAMMACK, Am. J. M. Sc. **175**:96 (Jan.) 1928.

Basing their opinion on 4,000 transfusions and recognizing three types of reactions following transfusion ([1] febrile reactions, with or without chills; [2] reactions resulting from wrong blood group and [3] anaphylactoid reactions) the authors found that when transfusions were given from nonfasting donors the patients in certain cases show a reaction and that when fasting donors were used a reaction did not occur. On one occasion, when transfusion was given two hours after the donor had eaten a hearty protein meal, the patient had a severe chill and fever reaction which began two hours after transfusion. Three hours later, hemoglobinuria was observed. Error in grouping of the bloods could not be discovered. The authors conclude that the evidence from the case suggests that some of the febrile reactions following transfusion may be produced by blood from nonfasting persons and that these reactions can be avoided by having donors fast for a period before transfusion. In their experiences, an overnight fast seems to be sufficient.

HENSKE, Omaha.

PSEUDARTHROSIS OF THE TIBIA IN YOUNG CHILDREN. RICHARD B. DILLEHUNT and JOHN F. LECOCOZ, J. A. M. A. **90**:1615 (May 19) 1928.

A case of pseudarthrosis of the tibia of nearly two years' duration in a child, aged 2½ years, is reported in which operative treatment resulted in securing bony union. A simple procedure is described which the authors believe useful when the fragments are within reasonable proximity. It is of interest to note that shortly after complete union had occurred the same tibia was fractured at a lower level. A splint was applied, and union was prompt.

KÖHLER'S DISEASE OF THE TARSAL SCAPHOID BONE. MORTON SELDOWITZ and LEW ZIMTBAUM, J. A. M. A. **90**:1617 (May 19) 1928.

The authors suggest that Köhler's disease of the tarsal scaphoid bone is a manifestation of rickets. The chemical analysis in their case suggested the presence of rickets. It is generally agreed regarding treatment that under rest and palliative care, healing takes place in from six to eighteen months. On antirachitic therapy, healing was produced in this patient in four weeks.

BONAR, Salt Lake City.

A STUDY OF ACUTE APPENDICITIS IN CHILDREN UNDER TWELVE YEARS OF AGE. C. W. WOODALL, New York State J. Med. **28**:322 (March 15) 1928.

Two hundred and ninety-five cases were analyzed to determine as far as possible the factors responsible for death, which occurred in 77.45 per cent.

In 155 cases, surgical aid was sought thirty-six hours after the onset. In 27.8 per cent, the patients were referred to a surgeon after sixty hours. While the mortality rate compares favorably with other reports, the writer believes that earlier surgical intervention and better surgical care might reduce the death rate to below 5 per cent.

PERINEPHRITIC ABSCESS IN CHILDREN. ADOLPH DESANCTIS and HENRY A. REISMAN, New York State J. Med. **28**:584 (May 15) 1928.

Seven cases are reported. In each, a mass was palpated and an abscess shown on operation. Five were definitely due to metastasis, four of the patients having had boils, superficial abscess or paronychia. In three cases the abscess was on the left side and of the three two gave evidence of irritation of the psoas muscle, which is characteristic when the abscess is on this side. Of the four cases in

which the abscess was on the right side, none showed irritation of the psoas. Early recognition and operation will materially lower the mortality rate. Three of the seven patients made a good recovery; four died.

AIKMAN, Rochester, N. Y.

NONTRAUMATIC LESIONS OF THE DIAPHRAGM IN INFANCY AND CHILDHOOD. HARRY C. OLMSTEAD, Northwest Med. **27**:169 (April) 1928.

So-called hernias of the diaphragm are of two types. The first or true hernia, in which the abdominal organs are covered with thinned out diaphragm, is seen almost exclusively in adults, and occurs at weak areas near the foramina. The second or false hernias do not have a hernial sac and are due to congenital defects of union of the several components of the diaphragm. These vary in extent; there may be a complete absence of one side of the diaphragm or a small deficiency may be apt to obstruct the bowel. The deficiency is most often left sided and when the eventration is large, the lung is often rudimentary. Diagnosis can often be made by physical signs alone, the presence of a changeable dulness and tympany being especially suggestive. The x-ray is the most important aid in establishing a certain diagnosis. Treatment is postural and surgical. Few reports of successful closure are extant. The operative mortality is high, but this is often because intestinal obstruction has already occurred. Reduction is performed through the abdomen in most cases, but the transthoracic route is becoming increasingly popular because there is no negative pressure to hinder reduction. Pneumothorax occurs after both operations.

Elevation of one side of the diaphragm is another anomaly detected by the x-ray. In this, one side occupies a high position due to a congenital or perhaps acquired atrophy of the muscle fibers. Possibly a lesion of the phrenic nerve might be causal. The mass may displace the thoracic organs and embarrass breathing and circulation. In the x-ray, the bowlike arch of the diaphragm is intact but occupies a high position.

A third defect is found at necropsy and is known as diaphragmatic grooving of the liver. These are disposed sagittally along the upper surface of the liver, usually in the right lobe. They have not yet been detected roentgenographically. They are believed to be due to difficult respiration or thoracic deformity.

SCOTT, Philadelphia.

NEUROBLASTOMA OF THE ADRENAL IN YOUNG CHILDREN. MARTHA WOLLSTEIN, Surg. Gynec. Obst. **46**:774 (June) 1928.

A review of the literature and a discussion of the primary suprarenal tumors is presented, and a series of nine cases of sympathicoblastoma is cited. In this series of nine cases, three tumors showed areas of ganglioneuroma in the tumor, and one such tumor metastasized extensively to the bones, dura and liver. The two others were removed by operation before any metastases occurred. Both of these children recovered from the operation, and one was alive seventeen months after removal of the tumor, the only one recorded to survive so long. In seven of the nine, the tumor proved inoperable when first discovered.

Clinically, the most rapidly fatal cases are those which present enlargement of the liver as the main symptom. Those tumors which metastasize to the bones frequently present swelling and discoloration of the lids of one or both eyes as the first symptom, the suprarenal primary tumor being found on palpation of the abdomen.

GALL BLADDER DISEASE IN YOUNG SUBJECTS. ALFRED H. POTTER, Surg. Gynec. Obst. **46**:795 (June) 1928.

A complete tabulation and analysis of cases of gallbladder disease in children under 15 years of age from the old and more recent literature are presented. The source of the case, age of the patient and the pathologic condition present are given

in detail. The author is of the opinion that the rôle of the infectious diseases of children are not accorded their proper share of the blame for the diseases of the gallbladder and biliary tract, and states that they are of great importance in the etiology of the diseases of these systems. He also believes that infections of the digestive tract, regardless of origin, must be considered the most probable origin of the infections of the gallbladder in the young, but this presumes a stagnation of the gallbladder.

G. H. JACKSON, JR.

ACUTE INTESTINAL OBSTRUCTION IN INFANTS. J. C. S. BATTLEY, Canad. M. A. J. **18**:562, 1928.

The author reviews the literature on intestinal obstruction. Two cases of intestinal obstruction in the same family, due to congenital anomalies, are reported.

MOORE, Omaha.

EMPYEMA IN INFANCY AND CHILDHOOD. LUDWIG SILBER, Monatschr. f. Kindrh. **39**:35, 1928.

Of twenty patients with pneumococcus empyema, all but three of which were under 1 year of age, the writer was able to save six. Of the various treatments recommended, he got the best results in the youngest children with repeated puncture and intramuscular injections of blood. In the older infants, the pleural cavity was also irrigated.

GERSTLEY, Chicago.

Miscellaneous

SUMMARY OF PROVISIONAL BIRTH, DEATH, AND INFANT MORTALITY FIGURES IN THE BIRTH REGISTRATION AREA: 1927. (Exclusive of Louisiana, Massachusetts, and Utah, from which complete transcripts for 1927 have not been received.) Department of Commerce, Bureau of the Census, Washington.

The Department of Commerce announces that birth rates for 1927 were lower than for 1926 in twenty-three of the thirty-three states for which figures for the two years are shown in the following summary. The highest 1927 birth rate (28.8 per 1,000 population) is shown for North Carolina, and the lowest (13.6), for Montana.

Death rates for 1927 were lower than for 1926 in twenty-eight of the thirty-three states shown for both years. The highest 1927 death rate (13.9 per 1,000 population) is shown for Vermont, and the lowest (7.1), for Idaho.

Infant mortality rates for 1927 were lower than for 1926 in thirty of the thirty-three states shown for both years. The highest infant mortality rate (125.8) in 1927 appears for Arizona, and the lowest (47.5) for Oregon.

Infant mortality rates are shown for both years for forty-eight cities of 100,000 population or more in 1920. For forty-two of these cities the 1927 infant mortality rates were lower than those of the previous year, the lowest 1927 rate (41.4) being for Seattle, and the highest (87.1) for Norfolk, Va.

THE FIRST THREE MONTHS OF LIFE. E. MORO, Internat. Clin. **2**:271 (June) 1928.

The first three months, called the "first trimenon," are characterized by marked lability of all functions. The infant still is an "unfinished" organism. Nutritional disturbances are especially severe at this time. The greater the rapidity of growth, the greater are the requirements and care of the building material. Tolerance for deviation from the normal conditions is less during the period when the infant grows most rapidly. "Dyspepsia acida" is seen during the first three months in breast-fed infants. The cause lies within the infant—increased peristalsis. The nervous system, supplying the gastric and intestinal apparatus and governing its

function, is especially irritable in this early period—the reason for frequency of pylorospasm at this time.

Tetany and rickets are uncommon in the first three months, probably due to the reserve supply of vitamin D. Psychic development is on a low level, and motor functions are primitive. If the young infant is placed on a pillow and the pillow is struck on each side, at first both arms spread far apart symmetrically, then approach one another slightly with somewhat jerking motions (Moro reflex). This phenomenon disappears after three months and is considered an atavistic motion—a natural clinging reflex.

MILO MILLER, South Bend, Ind.

A PLAN FOR THE REDUCTION OF DEFECTS IN MEN OF MILITARY AGE. R. A. MILLIKEN, Mil. Surgeon **63**:182 (Aug.) 1928.

In statistics gathered during 1917, it was found that of 2,753,922 men of military age, examined, 687,486, or nearly one-fourth, were rejected. In addition, 601,917 had various physical defects. This means that only one half of our young men are up to such a low physical standard as to be called merely "not defective." The author believes that incorrect body mechanics in childhood have a great influence on a production of more than half of these defects. It follows, then, that instruction in school and training of children in proper body mechanics and posture will produce a great reduction in body disability.

SANFORD, Chicago.

PEDIATRICS: METHODS OF EXAMINATION. ISAAC A. ABT, Wisconsin M. J. **27**:160 (April) 1928.

Physical examination of children comes first in order and importance; laboratory tests are secondary. Pediatricians must have enough knowledge of general medicine and of the other specialties to recognize borderline cases and refer them in time when necessary. The importance of the thymus gland is over-rated. The thymus is not an organ of internal secretion, and it rarely produces pressure symptoms. Heart murmurs without other cardiovascular symptoms are not indicative of organic disease.

JANNEY, Milwaukee.

A DISCUSSION ON ULTRAVIOLET THERAPY. Tr. Med.-Chir. Soc. Edinburgh M. J. **35**:41 (March) 1928.

Forty pages of this journal are occupied with the discussion by numerous members of the Scottish profession on the technic and results of ultraviolet ray therapy. Most of the speakers believe that the carbon arc lamps are superior to the mercury vapor lamps. Robert Aitken concludes that neither erythema nor nigmentation is necessary for producing good results. Jardine used both slow and ordinary dosages, and found in nonpulmonary tuberculosis, chiefly in children, that the red and white blood cells, the color index and the calcium, iron and iodine of the blood are all increased by treatment. The children are made happier and are willing to undergo long periods of rest; appetite, sleep and muscular tone are made better.

Lewis Thatcher believes that although results at the Sick Children's Hospital are good, they are not the equal of those at Rollier's Clinic and other Alpine winter resorts, where residence in an outdoor sunny climate has an added advantage. He quotes the work of Miss Mackay in the East End of London, where children under 18 months, artificially fed, all carefully supervised, were compared as to the additional effect of the mercury vapor lamp in 66 instances, with 137 controls. During the winter months the irradiated infants were happier and had better nutrition, muscle tone and skin—conditions which were maintained even after treatment was discontinued. Thatcher believes that infants under 4 months of age do not do well with irradiation. The emphasis should be placed on vitamins, a well-balanced dietary, fresh air and exercise.

Miss Todd presents two tables compiled from the Royal Hospital for Sick Children. In tuberculosis, the best results from light therapy occurred in servical

adenitis. Rickets comprises the largest number of any one group, and the effect of light treatment is good if conditions at home are made better. Emaciated infants do not respond to irradiation by a stimulation of metabolism, and the skin reaction may cause fever. Ultraviolet therapy should be used with caution because of serious ill effects in certain cases.

Dr. Lambie believes that therapy is indicated when there is reason to conclude that vitamin is not being absorbed adequately from the intestines. In tuberculosis, the ray may hasten deposition of calcium phosphate in the neighborhood of caseous foci and thus hasten the cure.

HEALTH AND PHYSICAL TRAINING. WILLIAM GEORGE SYM, Edinburgh M. J., Tr. Med.-Chir. Soc. **35**:117 (June) 1928.

Sym describes the work of the Committee of the Education Authority in dealing with the health and physical training of 60,000 children under its care. Each child is examined three times during his school life, at 5, 9 and 14 years of age. His complete record is studied, and the height, weight, nutrition and other features are compared with children generally. About 20 per cent of these children suffer from some defect. It has been found that only 26 per cent of the children who have been notified follow the request to have dental conditions corrected.

Most importance is placed on mental and physical deficiency and contagious diseases. The committee sees that children are properly classified and sent to the proper school, hospital or training home. These institutions in Scotland are mentioned, and the character of their work is briefly described.

NEFF, Kansas City.

INFANT MORTALITY AND MORBIDITY IN PORTO RICO. A. F. ISERN, Porto Rico Rev. Pub. Health. **3**:461 (May) 1928.

The infant mortality in Porto Rico during the years from 1922 to 1927 was 39,376 deaths (an average of 147 per thousand live births); of these, 31 per cent were due to diarrhea and enteritis; 18 per cent to respiratory diseases, and 17 per cent to congenital debility. The only important preventable contagious diseases were tetanus neonatorum, 6 per cent and malaria, 3 per cent.

SANFORD, Chicago.

CHILDHOOD AND THE MOVING PICTURE. ROUVROY, Rev. internat. de l'enf. **5**:29, 1928.

As director of the institute for subnormal children at Moll-Huttes, Belgium, Rouvroy has had occasion to note the effects of cinema performances on various groups of children. In an exhaustive psychocriminologic study, he launches a bitter indictment against the prevailing type of public picture shows and recounts his personal experiences with borderline children following attendance at these exhibitions. Rouvroy believes that all sorts of films are deleterious except those dedicated exclusively to children; he discounts the protection presumed to accompany censorship, as suggestive scenes of violence and crime are not deleted nor the highly improper tableaux of so-called social propaganda expunged. Physical damage through eye strain and great fatigue incurred through concentration of the child's attention uninterruptedly for two or three hours are secondary to the debasing influence on the social and moral health of those whose margin in this respect is narrow. Impressions are recorded in receptive minds which activate the subject later on into criminal states.

THE ANTISOCIAL FAMILY AND THE MALADJUSTED CHILD. VAJKAI, Rev. Internat. de l'enf. **5**:357, 1928.

One of the most helpful agencies of the International Union for Child Welfare, known as the "Save the Children Fund," has established an institution for maladjusted girls in Budapest. Only mental defectives and those with a criminal record

are barred from the privileges of the Lord Weardale Home. The children, now numbering 122, are collected by authorized investigators from districts in which the environment is demoralizing; from homes in which economic conditions preclude even elementary care and instruction, and from the ranks of the vagrant population which still constitutes an acute problem in most European cities. In reviewing the history and the subsequent behavior of these girls, it was found that 56 of the 122 could readily be adjusted to normal social life. They would have undoubtedly developed into law abiding citizens if given the advantages of a decent home. The remainder belonged to the antisocial group, whose maladjustment could be traced directly to the chaotic state of domestic life following the war. Illegitimacy, hostile stepfathers and stepmothers, grinding poverty and the utter lack of proper amusements have driven these girls to delinquency. Efforts to restrict the number of these unfortunates, an endeavor proving highly successful in England, Belgium and Austria, may be divided into two groups, one having for its object the prevention of delinquency through the timely discovery of the maladjusted child, and the other concerning itself more in the treatment of delinquency itself. It is claimed that 80 per cent can be given a moral foundation which will result in adequate cultural development, but the antisocial family cannot be expected to disappear from Europe until the almost fatal blow to its economic structure has been permanently relieved. Two principles are followed in this particular division of child welfare: (*a*) removal from the home and training in an institution; (*b*) allowing the child to remain where he is and endeavoring to readjust the entire family. The latter, of course, is the more effective solution and is recommended by the author.

AMESSE, Denver.

IODINE POISONING FOLLOWING THE USE OF IODIZED OIL 40 PER CENT IN THE BRONCHI FOR DIAGNOSIS. E. RIST, F. HORSCHBERG, G. E. H. ILL and J. RAULOT-LAPOINTE, Bull. et mém. Soc. méd. d. hôp. de Paris **43**:599, 1927.

Four days after two injections of iodized oil 40 per cent into the air passages five days apart, an iodine rash appeared. A stenosis of the bronchi of the right lung, probably congenital, was found with dilatation of the left bronchi. There was no albuminuria, but edema of the face and pharynx developed, and these were like the toxic effects of potassium iodide.

These symptoms continued about a week, and eight days after their onset considerable iodine was found in the urine.

AN EXTENSIVE ICE-CREAM POISONING. H. BRAUN and F. MÜNDEL, Klin. Wchnschr. **6**:1286, 1927.

In Offenbach on the Main, eighty-nine persons partook of ice cream in August, 1926, and eighty-seven became acutely ill. The average duration of the fever was slightly less than two days. No deaths are reported. The bacilli isolated from the ice cream, and from the blood, stools and urine of the patients were identified as *B. suipestifer,* an organism not generally regarded as pathogenic for man. It is believed that the great number consumed with the ice cream was a factor in causing illness. Some patients had herpes, roseolae and an enlarged spleen.

E. R. LE COUNT.

Society Transactions

AMERICAN PEDIATRIC SOCIETY

HOWARD CHILDS CARPENTER, M.D., Secretary

Fortieth Annual Meeting, April 30-May 1-2, 1928

HENRY L. K. SHAW, M.D., *Presiding in the Chair*

(Continued from page 412)

Third Session, 9 a. m., May 1, 1928

HYPERTENSION IN THE YOUNG. DR. SAMUEL AMBERG.

At the Mayo Clinic during a period of about eight years, twenty-five cases of increased blood pressure were seen in persons whose ages ranged from 6 to 16 years. No necropsies were obtained.

Usually, hypertension in childhood has been described as nephritic in origin. This was not true in some of our cases. Renal involvement may exist without impairment of renal function, and renal insufficiency can exist without abnormal urinary constituents.

If one considers a phenol red return of 50 per cent and more and a blood urea of 30 mg. per cent and less as indications of renal sufficiency, and more or less persistent albuminuria, presence of casts, erythrocytes, and pus cells in the urine in degrees greater than 1 on the basis of 4, as indicative of renal involvement, the cases at the time of observation may be classified as follows: (1) renal function not impaired and urinary data negative, eight; (2) renal function adequate, and urinary data positive, six; (3) renal function impaired and urinary data negative, two; (4) renal function impaired and urinary data positive, nine.

Group one contains three cases of coarctation of the aorta, in which discrepancy in the blood pressure in the upper and lower extremities existed, in addition to superficial pulsating arteries on the thorax. In one case the increased blood pressure was probably due to a definite cerebral lesion involving the left temporal lobe, with changes in the character of the fluid of the lateral ventricle. Some time after operation the blood pressure became normal. One of the remaining four cases of group one belong to the primary essential hypertensions; the other three, probably, to that type which Keith, Wagener, and Kernohan described as cases of malignant hypertension. Renal impairment is not the primary factor, nor is it necessary to complete the clinical picture. There seems to be widespread vascular disease, which depending on its extension, severity and localization, may cause disturbance in any organ. One of these patients, a boy aged 9 years, had had symptoms for five years. He seemed to be in excellent condition, and the renal tests gave negative results. Later, renal insufficiency developed. In the child, as in the adult, renal impairment with high blood pressure is not necessarily nephritic in origin.

The heart was markedly enlarged in six cases, in two of which cardiac decompensation was present. In one, the increased pressure in all probability was attributable to cardiac involvement. More pronounced peripheral arteriosclerosis was present in three cases. In some cases the capillaries of the nail fold presented changes. The eyegrounds showed marked changes in ten cases, slight changes in

eight and none in five. In one case a biopsy of the pectoral mucocele showed thickened arteries and arterioles, as well as other changes. Signs of cerebral involvement occurred in five cases, independent of headache and vomiting. The latter alone, or more frequently associated, were noted in fifteen cases. In one, the headache was unilateral. In four cases the blood pressure gradually became normal, while in the others, so far as is known, the increase was irreversible. Death is known to have occurred in ten cases; two patients are in poor condition and confined to bed.

DISCUSSION

DR. BELÁ SCHICK, New York: I shall mention only one kind of cardiovascular disease which I saw in combination with high blood pressure. These were cases of periarteritis nodosa.

An inflammatory process is found around all vessels, or sometimes is restricted to certain organs, like the vessels of the brain or kidney. The changes do not have to be so far progressed as to show symptoms of nodules. In certain cases the intensive inflammatory process in the different layers of the vessels leads to a marked narrowing of their lumen. Since many infectious diseases like diphtheria and rheumatic infection lead to so many vascular changes, one should bear in mind the possibility of finding more or less milder forms of periarteritis without the development of nodules. The clinical picture of periarteritis is bizarre, because so many different organs are involved. The combination of cerebral and kidney symptoms with high blood pressure is, in my experience, suggestive of periarteritis with or without nodules.

DR. KENNETH D. BLACKFAN: Mills and I first observed hypertension in persons with acute glomerular nephritis, and as the result of those observations concluded that the hypertension was due to a compensatory action on the part of the heart to maintain active cerebral circulation disturbed by the edema of the brain. Since then we have followed with more care the arterial tension in young infants and children.

I believe that one should look at hypertension as a symptom and, as Dr. Amberg pointed out, one of the conditions that may bring this about is found in the kidney. Hypertension is found in the acute hemorrhagic form of nephritis with cerebral edema, and as Dr. Green has reported recently, arterial tension in chronic diffuse nephritis of young infants. Dr. Parsons also called attention to the association of hypertension with chronic interstitial conditions associated with bony deformities (renal rickets).

We have also observed hypertension associated with congenital heart disease as well as in some forms of acquired heart disease.

A more interesting group, to me at least, than these conditions which are well recognized now in the child as well as in the adult, is the association of hypertension with conditions particularly affecting the brain. In a number of persons with encephalitis, hypertension has led us to attempt to reduce the arterial tension which we think is due to cerebral edema.

That this hypertension is explained as the basis of cerebral edema I think can be shown by the study of brains at autopsy and also by the response to treatment which is directed toward the reduction of hypertension.

An interesting case recently studied by Dr. McKahnn was that of a child, aged 10 months, who was suffering from lead poisoning and who during the course of an acute infection developed convulsions. On admission to the ward, he was in status epilepticus and showed papilledema of the optic nerves. The sutures of the skull were apparently relatively firmly united. The fontanel was about the

size of a quarter, but as the papilledema developed to the extent of 2 diopters the sutures became separated and the anterior fontanel enlarged to the size of a large silver dollar. During this period, there was a steadily arising arterial tension. As treatment was directed toward the reduction of the cerebral edema by the use of magnesium sulphate, the hypertension gradually subsided, and the fontanel returned to the original size as the signs of cerebral edema disappeared. That this was cerebral edema and hypertension probably due to a compensatory action of the heart in order to avoid anoxemia or to maintain adequate circulation, I think, can be shown by the fact that in other cases of toxic encephalitis due to lead, the brain has been found larger than the normal brain for the age, with flattening of the convolutions and the medullary cone phase, resulting from the edematous brain being pressed firmly into the cisterna magna.

Dr. D. Cowie: I should like to record a case of hypertension in a boy, aged 8 years, who came to our clinic in January, 1927, with a large tumor in the left upper quadrant of the abdomen. There was every evidence pointing to a tumor of the kidney and all the manifestations of hypertension of long duration; headache, vomiting, nocturia, albuminuric neuroretinitis, casts and increased leukocytes in the urine. The blood pressure varied between 220 and 230 systolic, and 100 and 180 diastolic. At operation on February 11 a polycystic kidney (papillifferous adenoma) was found. Dr. Coller carefully examined the other kidney and found it normal. Feeling that the pressure or some influence of the tumor had something to do with the hypertension, I had blood pressure records made during the progress of the operation. Before ethylene anesthesia the blood pressure was 190, systolic; 168, diastolic. It progressively fell to 122 systolic; 90 diastolic, seventy minutes later. The following morning it was 110; 90. Sixteen days later, on discharge, it was 120; 105. Very soon after the abdomen was opened, the pressure began to fall.

Data of further interest in this case were: The blood chemistry during the preoperative hypertension period was: nonprotein nitrogen, 39.4; carbon dioxide, 60.5 per cent by volume; chlorides, 412; creatinine, 1.5; sugar, 92 mg. per cent; cholesterol, 258 mg. per cent; serum protein, 8.6; phosphate, 3.8 and calcium in the serum, 10.5. Examination of the urine showed normal concentration and variation in gravity; phthalein, 50 per cent the first hour and 20 per cent the second hour. On February 11, the blood pressure before the ethylene anesthesia was 190, systolic; 168, diastolic; five minutes after anesthesia it was 200, systolic; 150, diastolic; ten minutes after it was 220, systolic; 160, diastolic; thirty minutes after, 200, systolic; 120, diastolic; sixty minutes, 140, systolic; 120, diastolic; seventy minutes, 122, systolic; 90, diastolic. On February 12, the blood pressure was 110, systolic; 90, diastolic; on February 13, 120, systolic; 70, diastolic; February 16, 118, systolic; 92, diastolic; February 19, 120, systolic; 100, diastolic; February 20, 110, systolic; 70, diastolic; February 22, 98, systolic; 74, diastolic; February 23, 122, systolic; 105, diastolic, and on March 3, 120, systolic; 105, diastolic. The patient was then discharged.

Dr. Henry Heiman, New York: I should like to ask Dr. Amberg whether he took into consideration the family history in these cases. As a rule, the hypertension in children of that type is supposed to be the familial type. I recall a case in the ward years ago in a boy 8 or 9 years of age who had a blood pressure of 160 and over. In this particular child, it was possible to prove the sclerotic condition of the peripheral vessels by the roentgen ray. He suffered intense abdominal pain, which was regarded as a facsimile of the intermittent claudication in the adult. The case was fatal.

DR. AMBERG (closing): With regard to Dr. Schick's question, I may say that Dr. Kernohan did not find periarteritis nodosa in his studies of the syndrome of malignant hypertension.

In regard to the remarks of Dr. Blackfan, I had one case of decompensated heart.

With regard to the rôle of edema of the brain in relation to hypertension, no doubt there are a number of cases in which such a relationship exists. Kahler distinguishes two types of hypertension due to cerebral involvement: the mechanical, in which increased intracranial pressure interferes with the cerebral circulation, and the lesional. In the case I mentioned, a definite localized lesion of the brain existed, which could be removed by a surgeon. The symptoms subsided rapidly after the operation and although the blood pressure remained high during hospitalization, it returned to normal after the patient returned home.

In regard to Dr. Heiman's comments, hereditary influences were not manifest.

FURTHER STUDIES ON THE FUNCTION OF THE INTESTINAL MUSCULATURE. DAVID MURRAY COWIE and F. H. LASHMET.

Confirmation of the work of Alvarez and his associates on the rate, amplitude, tone and metabolic gradients of intestinal longitudinal muscle, as demonstrated by the Cohnheim-Magnus method, is reported.

An attempt is made to classify the curves produced by the contraction of the intestinal segments in oxygenated Locke's solution. The various curves produced by longitudinal muscle seem to fall definitely into primary, secondary and tertiary groups, each succeeding group depending on the primary groups as a basis.

When the Trendelenberg method is used, the differentiation of the happenings in longitudinal tracings due to changes in circular muscle tone and rhythm are shown.

A classification of circular muscle contractions is given and the types of curves produced by narrow band and broad band stationary contractions, short, traveling peristaltic contractions and rush waves are described. It is shown that there is a rate gradient and a tone gradient of circular muscle; that the amplitude gradient of circular muscle is not constant, but is sometimes seen.

It is observed that empty segments, lying in Locke's solution, do not show circular contractions, while segments containing feces show circular contractions and peristaltic waves. Empty segments attached to our displacement apparatus do not show circular contractions, while segments filled with Locke's solution under hydrostatic pressure show stationary and traveling contractions.

Circular muscle contraction always precedes the fall in longitudinal muscle tone by about one fifth of a second. At low intraintestinal pressure (from 10 to 15 mm. of water) circular and longitudinal muscles contract alternately, but the longitudinal contractions are altered. They assume the secondary and tertiary types of contraction.

The confusing bizarre curves so frequently seen in tracings of longitudinal muscle, we believe, are easily explained by these observations.

We believe that studies of this kind are basic. We hope that they may help clear the way to a better understanding of the question that still seems to be awaiting the last word—"What is the mechanism of intestinal peristalsis?" We believe that until all the factors governing peristalsis and reverse peristalsis are known, therapy of gastro-intestinal dysfunction will not be on a sound and fruitful basis.

DISCUSSION

DR. CHARLES G. KERLEY: The study made by Dr. Cowie is of much interest to me for the reason that for several years I have been observing children presenting

difficult digestive problems by roentgen-ray studies. I have roentgenograms of three patients with severe colic which show contraction of the circular fibers with gas block between the contracting areas. In one case the contraction is so narrow that the roentgenogram looks as though the intestine had been tightly tied with a suture. Cases of entrospasm such as the one described are responsible for many cases of colic and are to be explained by the contraction of the circular fibers.

DR. COWIE (closing): Soon after I called the attention of Dr. Alexander of our department of surgery to this form of contraction, he informed me that he had seen it occur in the appendix. We are, of course, interested in any reports of this kind because it has been generally believed that it is characteristic of the intestines to cease to perform as soon as the abdomen is opened.

THE RELATION OF THE ALTITUDE OF THE SUN TO ITS ANTIRACHITIC EFFECT. DR. FREDERICK F. TISDALL and DR. ALAN BROWN.

In a study of the seasonal variation of the antirachitic effect of sunshine at Toronto, Ontario (latitude 43° 40′), a marked increase in the antirachitic effect was found to occur about Feb. 14, 1927. A similar sharp increase occurred between Feb. 13 and Feb. 20, 1928. In the autumn of 1927, a marked decrease occurred between October 10 and October 17. The altitude of the sun at noon at Toronto on February 14 is 33 degrees; on February 21, 35 degrees; on October 10, 39 degrees, and on October 17, 37 degrees.

A series of eight cages with four rats in each cage was exposed to the sun's rays two hours daily during March, 1928. Each cage was exposed at a different time of the day, the time so calculated that the maximum altitude of the sun remained constant for each cage. Cage 1 received rays from the sun up to an altitude of 25 degrees; cage 2 up to an altitude of 30 degrees; cage 3 up to an altitude of 35 degrees; cage 4 up to an altitude of 40 degrees, and cage 5 up to an altitude of 45 degrees. All of these cages were exposed in the morning. In the afternoon, cage 6 was exposed for two hours with the sun at a maximum altitude of 40 degrees, cage 7 with the sun at a maximum altitude of 35 degrees and cage 8 with the sun at a maximum altitude of 30 degrees. Examination of the inorganic blood phosphorus, percentage ash in the bones and roentgenograms of the long bones showed a definite increase in the antirachitic effect of the sun's rays with the sun at an altitude of 35 degrees and over.

A study of the geographic distribution of rickets shows that in the places in which rickets does not develop, in spite of poor hygiene and dietary conditions, the minimum seasonable altitude of the sun is usually 35 degrees or above. In some instances it was just below 35. Rickets occurs chiefly in the cities of the north temperate zone, north of 40 degrees north latitude. The minimum seasonal altitude of the sun at 40 degrees north latitude is 26 degrees. In Glasgow, Scotland, the sun is below an altitude of 35 degrees for six months of the year; in London, England, five months; in Toronto, Ontario, and Boston, four months, and in Baltimore, three months.

It would appear that a marked increase in the antirachitic effect of the sun's rays occurs when the sun reaches an altitude of 35 degrees and over. This information should be of value in determining the probable "rachitic season" for any city in the world.

DISCUSSION

DR. ALFRED F. HESS: Dr. Tisdall showed that the sunlight has to be considered not only from a quantitative but a qualitative point of view. One can make a table this way, as he has said, based on the altitude of the sun, and find

out in that way the geographic distribution of rickets throughout the world. One can make a similar table if one takes the annual amount of sunlight in the various cities; for instance, New York has approximately 2,500 hours of sunlight. London, as I remember, has about half as much, 1,200 or 1,300. Glasgow has the lowest amount. It has perhaps only 1,000 hours of sunlight. So, although there are qualitative differences, one can by this means construct a good table. I have a table composed of probably forty different cities throughout the world, and it is remarkable how the incidence of rickets runs parallel to the amount of sunlight in these places.

What is wanted is a measurement of the wave lengths. There are such records at the present time. There is an instrument of this kind in the laboratory at Tucson, Ariz., and another one, I believe, in a laboratory at San Francisco, which shows the different wave lengths of the solar rays and the intensity of these wave lengths.

I disagree with Dr. Tisdall's statement that wave lengths must be as short as 300 millimicrons to be antirachitic. That would mean that little protection is gotten from the sunlight in winter, for in a city like New York, there are a great many days when the wave lengths as short as 302 millimicrons do not reach the sidewalk. Those of 305 and 310 millimicrons also have antirachitic activity.

What is needed is a record obtained from recording thermometers. They are expensive and are not available, but they show the wave lengths at various times of the year in different localities.

One other point should be emphasized: usually, that the healing or protection against rickets may be somewhat different in children than in animals. For example rats are sensitive to rickets and chickens more so. In chickens the slightest amount of sunshine will bring about curative signs. So one cannot transfer these results exactly to children. It is true, no doubt, that in the winter infants are protected by sunlight, but not to the same extent that chickens or rats are.

I was disappointed when I placed infants out on the veranda in January or February several years ago. I happened to have poor luck; for those two or three weeks the weather was inclement and there was a great deal of cloudiness. I could not protect against rickets. I think that other means than winter sunlight will have to be resorted to if one wants to protect or cure infants with rickets in the large cities.

DR. HENRY J. GERSTENBERGER: One point that Dr. Tisdall made should be emphasized, namely, the fact that rickets does develop in the summer if the human infant does not get out into the sunlight, and that the human infant does not get out in the sun frequently, especially when he is young. The newly-born infant, especially after he is 2 weeks old, needs the antirachitic factor far more than the infant 10 months old; the young infant frequently is kept indoors in the summer because of the excessive heat. Unquestionably, rickets develops in this country during the summer, and it is my opinion that this fact is not appreciated as it should be, possibly because the rickets does not, as a rule, reach a severe degree.

DR. F. S. CHURCHILL, Milton, Mass.: I should like to ask Dr. Tisdall if he has checked the meteorologic record as to the amount of cloudiness in Toronto at different times of the year and different months and if it has had any effect on rickets?

DR. FREDERIC W. SCHLUTZ, Minneapolis: I should like to ask Dr. Tisdall whether he has any data on some of the South American cities situated near the tropics, such as Rio de Janeiro and Lima and La Paz. These cities have, I believe,

quite an incidence of rickets in spite of the fact that there is intense sunlight during a large part of the year.

DR. TISDALL (closing): I can readily see what Dr. Hess had in mind. In his own paper he is going to say that ergosterol must be used, as the sun is not quite effective enough.

There is one point with regard to the cloudiness. Last year I gave a short paper before this society in which I showed that the antirachitic effect of skyshine is approximately one-half that of sunshine plus skyshine. The clouds may reduce this somewhat; still, on a cloudy day if the sun is more than 35 degrees the antirachitic effect is still great.

Dr. Hess mentioned the effectiveness of different wave lengths. In work done at the Corning glass works by Dr. Gage in conjunction with the physics department at Cornell it has been shown that the most effective wave length is 296.8. I think that probably Dr. Hess is right when he says that wave lengths longer than 302 are effective.

Dr. Hess spoke about measurements of the amount of ultraviolet rays. In talking with Dr. Abbott of the Smithsonian Institution regarding the instruments in use at the present time, I found that he is convinced that they are not measuring the wave lengths we want in the way we want them. The only instruments which their institution has are spectroscopes, which have to be pointed directly at the sun. Measurements of the sunlight alone are not wanted. Measurements of the sunlight plus the skylight, the rays an infant gets when outdoors, are wanted. An instrument which will measure those rays is the photo-electric device. But unfortunately it measures wave lengths up to and longer than 320. We have shown that the wave length at 320 is of little value. Dr. Abbott is interested in this problem and is starting to devise an instrument which will measure the wave lengths we want, and I think when he gets it made he will send one to Dr. Hess and myself, and possibly we can find out how the New York and Toronto waves are coming through.

It is obvious that this experimental work cannot be done with infants. I do not know how much value we can put on this work in regard to infants, but it is the best we can do under the circumstances.

In regard to Dr. Churchill's question, we have kept a record of the cloudiness but not of the humidity. Of course, the haziness may be a factor.

In answer to Dr. Schlutz, I do not know the latitude of the cities he mentioned. I think that probably some of the patients in those cities did not go outside and obtain the strongly antirachitic rays of the sun.

CLINICAL EXPERIENCES WITH IRRADIATED ERGOSTEROL. DR. ALFRED F. HESS.

About a year ago, in collaboration with Windaus, I reported that ergosterol, a sterol obtained from yeast or ergot, developed remarkable antirachitic activity following subjection to ultraviolet rays. Further investigations have shown that as little as 1/20,000 mg. as a daily dose is sufficient to protect a rat from rickets. Clinical experiences with infantile rickets have served to confirm these laboratory tests. From 2 to 4 mg. a day of irradiated ergosterol will cure rickets, as evidenced by clinical, roentgenologic and chemical criteria. The signs of healing are exceptionally rapid; within two weeks the blood phosphate or calcium may be definitely raised and calcification may be evident by means of the roentgen rays. Especially to be noted is the disappearance of craniotabes, which may take place in a week or two. Tetany reacts as favorably to this medication as rickets does. As the result of giving irradiated ergosterol, the calcium or phosphorus levels may be raised considerably above the normal.

In view of this fact, as well as because the effect of irradiated foods and sterols has been studied for so short a time, these substances should not be given in uncontrolled amounts. The tendency of physicians and pharmaceutical concerns to recommend preparations of irradiated ergosterol in amounts which are many hundred times the equivalent of cod liver oil is to be deprecated as fraught with dangers yet unknown and unsuspected.

DISCUSSION

DR. ROYAL S. HAYNES, New York: I feel that Dr. Hess has rendered a service in bringing out the possibility of giving too much of this potent preparation. There is little need to urge its use by anyone who has been fortunate enough to have employed it. It is one of the most active agents that I have ever encountered. I have used a good deal of it this winter, and I can substantiate all that Dr. Hess has said as to its beneficial effects. I have not happened to use it in rickets or in tetany but have employed it when cod liver oil or the ultraviolet ray was indicated. In all these conditions it has been more than satisfactory. It seems definitely to raise the resistance of the individual to infection and to create a condition of well-being which evidences itself in improved appetite, increased desire for activity and a fine, clear skin. I feel sure that many uses will be found for it in older children in whom a need for vitamin D has not previously been recognized, if this is what it is. But its very excellence and the ease of its administration will make its use so general in the next few years that this note of warning as to overdose is of great value, for it should prevent an indiscriminate use of ergosterol, the indifferent or bad results of which would militate against the confidence this substance deserves.

Dr. Hess probably has seen the report of Kreitmair and Moll (München. med. Wchnschr. **75**:637, 1928) that they have been able to cause death in animals by feeding relatively large doses of irradiated ergosterol. Various animals were used.

During the summer of 1927, I had occasion to visit Professor Moro and Dr. Gyorgy at the University of Heidelberg and through their courtesy received some irradiated ergosterol put up in oil, which they had found satisfactory in the cure of rickets.

During the past month Dr. Hartman and I have used this material in the treatment of rickets with and without spasmophilic symptoms. The dose was smaller than that used by Dr. Hess, namely, 2 mg. daily, and the results obtained were remarkably good, as the protocol will show.

Case 1. N. J., aged 1 year, milk healing rickets, marked spasmophilia
Cathodal opening contraction normal in 5 days, rickets healed in 3½ weeks
Blood: Before treatment, calcium, 5.0; phosphorus, 7.0
5 days treatment, calcium, 9.3; phosphorus, 7.5
21 days treatment, calcium, 10.8; phosphorus, 6.1

Case 2. W. M. J., aged 17 months, moderate rickets, healing, marked spasmophilia
Cathodal opening contraction normal in 5 days, rickets healed in 3½ weeks
Blood: Before treatment, calcium, 5.1; phosphorus, 5.5
7 days treatment, calcium, 10.2; phosphorus, 4.6
25 days treatment, calcium, 10.4; phosphorus, 5.4

Case 3. B. J. C., aged 14 months, moderate rickets, healing (?), mild spasmophilia
Cathodal opening contraction normal in 4 days, rickets healed in 3 weeks
Blood: Before treatment, calcium, 7.3 - 4.3
13 days treatment, phosphorus, 10.9 - 6.9

Case 4. P. L. H., aged 13 months, mild rickets, probably no healing
Rickets healed in 4 weeks
Blood: Before treatment, calcium, 10.4; phosphorus, 2.8
22 days later, calcium, 10.2; phosphorus, 5.3

Case 5. E. T., aged 1 year, moderate rickets, probably no healing, mild spasmophilia
Cathodal opening contraction normal in 2 days, rickets three-fourths healed in 4 wks.
Blood: Before treatment, calcium, 5.9; phosphorus, 2.2
11 days treatment, calcium, 9.6; phosphorus, 3.9
24 days treatment, calcium, 10.0; phosphorus, 5.3

DR. FREDERICK F. TISDALL: Dr. Hess mentioned that the phosphorus increases to 10 mg. in some of the cases, and stated that he never saw that in normal cases before. Out of several thousand determinations I have also never seen blood phosphorus or serum phosphorus in normal patients anywhere near that concentration. One must remember the dangerous results produced by the parathyroid extract when it increases the calcium to about double the normal concentration in the serum. Here is a concentration of phosphorus nearly double the normal amount, and that one fact alone would make it appear that there are certainly some possible dangers in the use of ergosterol.

DR. SAMUEL W. CLAUSEN, Rochester, N. Y.: I should like to ask Dr. Hess whether he has found unirradiated ergosterol devoid of antirachitic activity; whether he regards ergosterol as the antirachitic provitamin or whether it is some other sterol; and why the clinical dose which he uses is relatively so large. This dose is about 100 times that which would be given if it were calculated from the curative or protective dose for the albino rat.

DR. B. RAYMOND HOOBLER: Has any work been done in attempting to find the optimum quantity of cod liver oil or the optimum quantity of ultraviolet rays used in the treatment? It seems that in a procedure which is so prevalent as the use of the ultraviolet ray and cod liver oil that we ought to be advised by those doing the intensive work on the subject as to something of the limits to which we might go from the minimum to the optimum.

Dr. Hess made the statement that there would not be any danger in large doses of cod liver oil, and he also said that he did not see that there was much danger, except perhaps burning the child, from the constant use of the ultraviolet ray. It strikes me that there are some limits to which the average pediatrician ought to be informed in relation to the optimum quantity of these two methods of administering vitamin D.

DR. HENRY HEIMAN: I am glad that Dr. Hess gave the sound warning on such an important potent drug. In fact, the same thing obtained when insulin was first introduced, and I am glad he also mentioned thyroxin. The only way thyroxin acts in normal persons as a potent drug is by a toxic action, and in that way may produce fever, tachycardia and actual poisoning, and diminish the weight of the person. So, extreme caution should be exercised in the use of ergosterol.

DR. CHARLES HENDEE SMITH: How rapidly can the calcium be raised with this preparation? Most of the cases reported were over a period of several days. In a case of tetany, for instance, is one justified in relying on ergosterol to raise the calcium rapidly? I have been a little afraid to rely on it entirely and have continued the older treatment for acute forms.

DR. HESS (closing): Dr. Kerley, as well as Dr. Tisdall, asked whether there was any physiologic effect of the high phosphorus. I did not note any, but I think that it may be dangerous to have a percentage of phosphorus twice as high as normal. I was looking for evidences of tetany, because sometimes if one raises the phosphorus there is a tendency to tetany, but I did not notice any signs. I believe that any dose which increases the phosphorus to this extent is contraindicated. Collip's preparation as well as hydrochloric acid and calcium and ammonium chloride will control tetany quickly. The ergosterol is of value in tetany but does not act as quickly as some of these preparations.

The increase in calcium does not last long, although it persists as long as or longer than the high calcium brought about by Collip's preparation. At present, in view of the fact that the possible dangers of ergosterol are not known, I should hesitate to use high doses in order to cure a patient with tetany.

The question was asked whether I consider ergosterol the provitamin. I have kept away from the terms provitamin and vitamin, questions of nomenclature. I do not believe that it is a provitamin, if I may use the term, because it has been proved that a digitalis derivative can also be activated. Bials has stated that cholesterol itself can be activated to a certain extent, and I believe that there will be other sterols which may be activated by means of ultraviolet rays. It may be that this substance acts as a catalytic agent. One can hardly conceive of 1/20,000 mg. or less dispersing into the various joints of the body and bringing about calcification. There is some discrepancy between the size of the dose of cod liver oil and that of the irradiated ergosterol, but this may have to do with the absorption or with changes undergone in the intestine.

Cod liver oil works by the subcutaneous route as irradiated ergosterol does, so one would infer that its effect is not directly on the gastro-intestinal canal as has been suggested.

In regard to the optimum dose of cod liver oil and of the ultraviolet radiation it should be borne in mind that cod liver oil itself varies greatly. In Newfoundland, in summer, one can get some cod liver oil that is twice as strong as other oils. I have found cod liver oil at other seasons which is sixty-four times as potent as high standard cod liver oil. My rule is to give a young child one and a half teaspoonfuls of cod liver oil and when the child is 2 or 3 months old to increase the amount to three teaspoonfuls. I know that this differs somewhat from Dr. Gerstenberger's method.

In connection with ultraviolet irradiation, in addition to burning there are other dangers. The children who are in most danger are those who do not burn. If a child begins to get erythema or to burn, no one will proceed much further. But those in whom the radiations go through into the tissues or the blood are the ones who are in danger and who are apt to get too large doses. When one cannot induce erythema with the usual dosage, it is dangerous to proceed further.

In regard to premature children, I may state that one of the slides illustrated an instance of a premature infant greatly benefited by irradiated ergosterol. Cod liver oil, in my hands, has generally failed in the treatment of premature infants.

THE CURATIVE EFFICACY IN HUMAN RICKETS AND RACHITIC SPASMOPHILIA OF SINGLE WEEKLY EXPOSURES TO THE QUARTZ LAMP. DR. HENRY J. GERSTENBERGER and DR. J. I. HARTMAN.

The report presented is based on the study of the therapeutic efficacy of single weekly exposures to the quartz lamp in thirteen patients with human rickets and rachitic spasmophilia. The erythema unit dose as determined by the method of Rost and Keller was used as the specific basic therapeutic unit. With the quartz lamp used by us this meant exposing the infants at a distance of 80 cm. for ten minutes. In the first group, which consisted of seven colored infants, the exposure was limited either to the front or the back and alternated at the next weekly treatment. In the second group, which consisted of five colored infants and one white infant, the same dose used for the first group was applied once a week to both front and back. In the case of the white infant, however, only one-half erythema unit dose was given in this manner. Tables 1 and 2 present the data in detail and show that with both methods, satisfactory therapeutic results were obtained. It is believed that the exposures with the second group, however, were more satisfactory, and it is suggested that this method be followed.

The object of the investigation was to avoid exposing the infants to unnecessarily large doses of ultraviolet rays, to simplify the schedule and to economize the whole procedure.

TABLE 1.—*Rickets Treated with Mercury Quartz Vapor Lamp*

Time, 10 Minutes; Distance, 80 Cm.; Frequency, Weekly (Front and Back Alternate Weeks)

				Period Before Treatment						Period After Treatment					
					Blood						X-Ray		Blood		
Name	Color	Age	Diagnosis	Duration	Week	Calcium	Phosphorus	Duration of X-Ray Healing	Cathodal Opening Contraction	Progressive Healing at Beginning of Treatment	Cathodal Opening Contraction >5	Beginning Healing	Complete Healing	Week	Calcium	Phosphorus
M. H.	Colored	2 mo.	Mild rickets.....	10 wk.	1	6.5	5.9	4 wk.	3	No	3 wk.	3 wk.	6 wk.	3	9.6	6.3
					10	7.6	4.4							6	12.6	7.0
A. G.	Colored	7 mo.	Mild rickets.....	5 wk.	1	4.3	5.5	3 wk.	4	No	3 wk.	2 wk.	5 wk.	2	9.1	6.6
					5	6.4	4.5							4	9.6	6.2
G. G.	Colored	12 mo.	Marked rickets...	10 wk.	1	7.2	2.2	7 wk.	>5	No	.....	3 wk.	11 wk.	3	9.3	4.0
					7	9.6	2.4							12	9.9	5.0
E. W.	Colored	12 mo.	Moderate rickets	8 wk.	1	5.3	5.1	None	3	No	3 wk.	4 wk.	8 wk.	2	7.3	5.0
					6	6.4	4.1							8	10.6	6.8
J. H.	Colored	8 mo.	Moderate rickets	5 wk.	1	8.8	1.6	4 wk.	>5	No	.....	4 wk.	7 wk.	2	9.7	3.5
					3	8.7	1.7							6	10.6	5.0
P. N.	Colored	17 mo.	Mild rickets.....	4 wk.	1	8.9	4.0	.....	2	Yes	1 wk.	.....	5 wk.	5	10.2	6.9
					4	6.3	4.8									
J. O. B.	Colored	24 mo.	Marked rickets...	3 wk.	1	9.0	5.8	.....	2	Yes	2 wk.	.....	12 wk.	3	6.9	6.5
					3	5.2	6.2							12	8.9	7.2

TABLE 2.—*Rickets Treated with Mercury Quartz Vapor Lamp*

Time, 10 Minutes; Distance, 80 Cm.; Frequency, Weekly (Front and Back)

				Period Before Treatment						Period After Treatment					
					Blood						X-Ray		Blood		
Name	Color	Age	Diagnosis	Duration	Week	Calcium	Phosphorus	Duration of X-Ray Healing	Cathodal Opening Contraction	Progressive Healing at Beginning of Treatment	Cathodal Opening Contraction >5	Beginning Healing	Complete Healing	Week	Calcium	Phosphorus
R. L.	Colored	9 mo.	Marked rickets...	8 wk.	1	8.9	2.3	None	>5	No	.....	3 wk.	8 wk.	3	0.2	3.2
					8	10.0	1.6							8	10.1	5.0
C. C.	Colored	10 mo.	Mild rickets.....	5 wk.	1	6.1	5.4	None	4	No	1 wk.	2 wk.	5 wk.	2	9.2	6.0
					4	6.3	4.5							5	9.5	6.1
R. R.	Colored	5 mo.	Moderate rickets	4 wk.	1	8.2	2.4	2 wk.	>5	No	.....	2 wk.	5 wk.	2	10.6	5.6
					3	8.0	3.5							5	10.7	5.7
R. H.	Colored	4 mo.	Moderate rickets	1 wk.	1	10.3	3.7	None	>8	No	.....	3 wk.	6 wk.	2	10.4	4.4
														6	10.8	5.9
W. R.	Colored	5 mo.	Moderate rickets	.....	1	6.0	3.4	.....	1	Yes (?)	1½ wk.	3 wk.	6 wk.	2	7.9	4.8
														4	10.0	5.6
J. M.	White	9 mo.	Moderate rickets	.....	1	6.3	3.4	.....	1	Yes (?)	1½ wk.	3 wk.	6 wk.	2	7.5	5.1
														4	10.0	6.8

We believe that the advantages of the method of quartz lamp ultraviolet therapy proposed are the following:

1. The number of exposures are reduced to one a week.

2. The erythema produced by the doses employed by us as given in the foregoing paragraphs for both colored and white infants is so slight that the skin is as ready to benefit from the second exposure as it was from the first. The same protection of the skin can be obtained for fair skinned white infants without decreasing the efficacy of the therapy below a satisfactory level by reducing the exposure to one half of an erythema unit dose. For white infants of darker hues, somewhat more than one half of the erythema dose and somewhat less than the full unit erythema dose may be necessary.

We believe it impractical to expose a limited part of the body surface in infants. Such a procedure requires the constant attention of an attendant, whereas when the infant is placed either on its back or on its abdomen it usually remains in this position without restraint or much supervision. Furthermore, as the dose required to produce therapeutic results changes the skin so slightly, there really is no need for making the time interval of exposure of the various skin surfaces greater than those that we have adopted.

CONCLUSIONS

1. Observations in thirteen rachitic spasmophilic infants show that weekly exposures to the ultraviolet rays produced by the quartz lamp in doses of one erythema unit, as determined by the method of Rost and Keller, for colored infants and less for white infants to both front and back brings about healing in practically the same time required by the heavier schedules generally used at present.

2. Because of the simplicity and economy of this arrangement and because of the slight change produced by such exposures to the skin, the adoption of this schedule as a routine procedure in the prevention and cure of rickets and rachitic spasmophilia by the use of the ultraviolet rays is recommended.

3. An increase in spasmophilic symptoms and a lengthening of the time period at which the cathodol opening contraction was > 5 were not observed as a result of the quartz ultraviolet schedule that we used in the rachitic infants manifesting spasmophilic symptoms. This observation does not lessen the need and therapeutic value of such measures as calcium chloride, ammonium chloride and magnesium sulphate in the active stages of rachitic spasmophilia.

DISCUSSION

Dr. A. Graeme Mitchell, Cincinnati: Clinicians must not only know that a treatment is effective but must be aware of possible dangers of overtreatment. It is therefore necessary to possess knowledge of the minimum treatment which will be effective.

In Cincinnati we have been working along somewhat the same line as Dr. Gerstenberger, but we have been interested in the prevention of rickets as well as in the cure of it.

Dr. Greenebaum, Dr. Selkirk and others have been studying a group of about 500 infants and have found that a comparatively small amount of ultraviolet light from artificial sources if given irregularly will prevent rickets. These figures are now being analyzed and will be presented at the meeting of the American Medical Association.

DR. BENJAMIN KRAMER, Brooklyn: Dr. Gerstenberger's paper raises an important point, namely, the delayed effect of antirachitic therapy. In much of the literature on the treatment of infantile rickets it is found that if definite rickets is shown roentgenographically and the blood shows what is interpreted as evidence of activity, treatment is begun without a preliminary period of observation. Within a period of one or two weeks, marked evidence of healing is obtained. The observations of Dr. Gerstenberger and Dr. Hartman would seem to indicate that evidence of healing may appear several days after irradiation, although treatment has not been applied during the interval.

A little more than a year ago we began the study of the antirachitic effect of irradiated cholesterol. In controlling our results we found not infrequently that the untreated children showed some evidence of healing.

I recall one paper which appeared in the *Journal of Metabolic Research* on the effect of feeding cod liver oil concentrate as compared with that of the oil itself. At the end of three weeks little if any healing was observed. A concentrate of cod liver oil was then administered, and within two weeks striking results were obtained. As a rule, following the administration of cod liver oil in the usual doses, healing begins at the end of three weeks and is marked at the end of four or five weeks. It is reasonable to suppose that the concentrate was begun just at the time when the cumulative effect of the cod liver oil was about to become evident.

I think that much of the work on the antirachitic effect of various agents must be reviewed carefully with these facts in mind; namely, that there is a tendency toward spontaneous healing, especially in older children, and at certain times of the year, and that all children on whom the antirachitic effect is tried should be under observation for a preliminary period so one can be sure that healing is not taking place as a result of the previous accidental administration of some antirachitic factor.

DR. B. RAYMOND HOOBLER: It is well to bear in mind that, with the large amount of discussion that is going on among the laity, particularly in relation to ultraviolet rays and cod liver oil, one should warn against a too general use of these therapeutic agents.

Not long ago I sat in on a conference with a prominent physicist from Chicago. He said he believed that a proposition had been made by one of the prominent manufacturers of lights that these lights should be placed in a large number of school buildings and that under certain supervision, whether satisfactory or not (we do not know) this light should be administered to the school children. This prominent physicist was not in any way a supporter of such a method. He believed that there should be careful work done in a suitable school to make sure just what methods should be used, so far as the school children were concerned.

Dr. Gerstenberger has given an excellent guide in determining, at least, the minimum quantities that should be given, and I think that whenever the subject of this general use is brought up pediatricians should be loath to put their approval on it, because then it will get into the hands of the laity, then into the hands of certain persons who are not adept in doing the work, and worse results will come than if it were kept within the field of the pediatrician.

I do not think that the minimum dose has been established. The fact has been established that once a week an erythema dose is sufficient and that is much simpler than the schedule in vogue at the present time.

DR. GERSTENBERGER (closing): I was interested in what Dr. Mitchell had to say about his preventive effort. It is not clear whether Dr. Kramer was agreeing with me or criticizing our procedure.

I wish to emphasize the importance of this point to which we called attention a year ago: unless one observes the course of the rickets in the roentgenogram and in the blood for a period of about three weeks after admission and before giving treatment, one might get credit for bringing on the healing observed without deserving it. The healing may in reality be due to something which was given the child before it was admitted to the hospital. However, if one has had an extensive experience, it is possible to judge dependably from the rapidity and extent of the healing process after the administration of the antirachitic factor whether the healing was due entirely to the therapy in the hospital or not.

Before one proceeds in this fashion, one must have had a great deal of experience.

AN ATTEMPT TO DEFINE THE SYMTOMATOLOGY OF VITAMIN B DEFICIENCY IN INFANTS. DR. B. RAYMOND HOOBLER.

From personal observation while visiting the tropics and from the existing literature, the symptomatology of infantile beriberi is set forth as follows:

1. Early gastro-intestinal upset, with vomiting and constipation, with consequent anorexia and loss of weight occurs.

2. The infants are restless and fretful.

3. They are pale and the skin has a waxy tinge.

4. There is a change in the quality of the cry. It is usually whiney, feeble, plaintive and strangely altered. None of the normal tone qualities are present. The voice may become entirely lost.

5. At times the eyes may become puffy, and edema of the extremities or general anasarca may be present.

6. There is a reduction in the amount of urine. The diapers are wet only once or twice a day and then with only scanty amounts of urine.

7. Acute attacks of colicky pain occur, during which the child becomes rigid and cyanotic.

8. Occasionally there may be symptoms referable to meningeal irritation such as choreic movements, twitching of the face, slight rigidity of the neck, general spasticity, squint eye and even convulsion. Lumbar puncture shows a normal spinal fluid.

9. Muscle tenderness, especially over the muscles of the calves, anesthesia over the shins and reduced patellar reflexes are present. A general weakness of the limbs with seldom a complete loss of function occurs.

10. The foregoing symptoms occur most frequently at or before the age of 3 months in infants breast-fed by mothers whose diets are deficient in the antineuritic substance vitamin B.

11. If this diet is persisted in, the child dies with symptoms of cardiac failure.

It is conceded at the outset that true infantile beriberi rarely, if ever, is seen in this country, but with the increasing knowledge of lack of vitamin B in the common articles of diet for nursing mothers and in the diets of infants artificially fed, it would seem that some of the symptoms of true infantile beriberi may be found in infants suffering from a partial deficiency of vitamin B. It was with the clinical picture of true beriberi in mind that observations were begun in order to try and formulate a group of symptoms which might be attributed to a partial deficiency.

Two questions were considered as important. First,

Could a partial deficiency cause symptoms? This is answered in the affirmative by quoting such authorities in the field of nutritional diseases as McCollum, McCarrison, Vedder and Sure. Second,

Does a partial deficiency of vitamin B exist in diets of young infants, either nursed or artificially fed? The chief articles in such diets are human and cow's milk, syrup, sugar and cereals with milk, none of which, with the exception of milk, contain vitamin B; and both human and cow's milk has been shown to be relatively low in this substance. Infants whose previous diet seemed to indicate at least a partial deficiency in vitamin B were given a substance in vitamin B and the effect of such additions studied.

From the data thus obtained, I have constructed the following mental picture of an infant whose diet is partially deficient in vitamin B: A pale, undernourished, fretful, whiney, spastic infant who consistently refuses much of its food.

SUMMARY

1. From personal observation and from various sources in the literature, symptoms of outspoken cases of infantile beriberi as they occur in the Philippine Islands have been presented.

2. It is conceded at the outset that such outspoken cases do not appear in infants of the United States but that owing to the type of the present American diet there is a partial deficiency of vitamin B in the diets of nursing mothers and in infants artificially fed on cow's milk, sugar and cereal mixtures.

3. Such a partial deficiency of vitamin B in the dietary may cause profound systemic changes, which in the course of development may produce a symptomatology analogous to that of a complete deficiency.

4. A group of symptoms appearing in infants believed to be on a diet partially deficient in vitamin B were caused to disappear on the addition of brewer's yeast concentrate in suitable quantities to the diet without any other change being made.

5. This symptom complex consists of anorexia, loss of weight, spasticity of the arms and legs, rigidity of the neck, restlessness and fretfulness.

6. Pallor with low hemoglobin is present.

DR. ALFRED F. HESS: This is a question which has been raised by biochemists at various times during the past ten years or more—that of the requirement for infants. It seems to me that it can be answered only by studies on children. When it comes to the larval form, subacute or latent types, they can only be studied on infants.

About ten or twelve years ago, I fed a large series of infants and young children yeast. That was at the time when it was not known whether yeast was of value for scurvy. I found that they made a sudden gain for about two weeks but that the gain was not great thereafter. I also found that it did not make much difference what diet they had been on; a number of children 2 or 3 years old had been getting vegetables and nevertheless showed a marked gain after the yeast was given, so that it is questionable whether the effect was due to the vitamin B that was added. The question is an open one whether children are getting enough vitamin B, but this can only be answered by observations on infants.

DR. HOOBLER (closing): I would like to suggest, in answer to Dr. Hess, that the reason why outstanding cases are not seen is because in practically all the diets of children in this country there is a small quantity of vitamin B. There is never a true deficiency such as exists in the Philippine Islands. But a much more serious and difficult problem has to be faced, that of a partial deficiency. If it does not develop in an outstanding case of beriberi, one is apt to think that it does not have a relation to disturbances of nutrition or nervous phenomena such as are seen in many children.

THE DISTRIBUTION OF THE GLOBULIN AND ALBUMIN FRACTIONS IN BLOOD AND URINE IN NEPHROSIS: A PRELIMINARY REPORT. DR. F. W. SCHLUTZ, DR. W. W. SWANSON and DR. M. R. ZIEGLER.

The chronic kidney disease known as nephrosis or tubular nephritis is a distinct clinical entity. An outstanding clinical characteristic of the disease is absence of hematuria and a variable degree of edema associated with extensive proteinuria.

Little is known of the etiology of the disease. The primary cause is not renal but is extrarenal and only secondarily leads to pathologic change in the renal tubules. Focal infections, especially about the region of the head, seem to play a rôle in the development of the disease.

The initial appearance and all subsequent exacerbations are almost always associated with some infection. Extensive proteinuria is a fairly constant characteristic of nephrosis.

The object of our investigation was the study of the distribution of the plasma protein fractions in the blood with simultaneous determinations of the kind and amount of protein excreted in the urine.

Three cases of nephrosis in various stages of the disease were studied over varying periods. Studies of this kind have not been reported for the young child. There are a few reports on adults.

The following methods were used in the investigation: The plasma proteins were fractionated according to the method of Berglund and macro-Kjeldahl determinations made on the filtrate after fractionation. Cholesterol was determined according to Bloor's method. The total nonprotein nitrogen was determined by the method of Folin. For the determinations on the urine, the concentration of sodium sulphate used for separating globulins and albumins, as described by Berglund, was used. The removal of all the proteins from the urine was accomplished by Folin's precipitating agents which he uses for blood. The results were checked by the heat method described by Kingsbury and Swanson. The total nonprotein nitrogen in the urine was determined by the macro-Kjeldahl method. Fat was determined by Soxhlet extraction.

The diet of the patients was practically salt-free and liberal in protein. The therapy used consisted in the removal of all apparent or suspected foci of infection, the liberal use of diaphoresis and certain diuretics such as diuretin and merbaphen with ammonium chloride. Not any particular form of therapy is efficacious.

The results of the experimental work showed that the plasma proteins for the three cases presented are low. The albumin globulin ratio is low. In two instances, there is an inversion of the relationship. There was marked increase of the cholesterol in each one of the cases.

As regards the urine, marked fluctuation was observed of the total amount of protein excreted from day to day, the percentage ranging from 0.86 to 22.55 Gm. a day.

As a rule, more albumin than globulin is excreted, but this ratio may be entirely reversed.

The point of greatest interest brought out in the urinary examinations is the fact that the kidney in tubular nephritis excretes globulins as readily as it does albumins, and at times even in increased amounts. Just what brings about this increased permeability of the kidney tubules for globulins in this condition is difficult to explain. In severe cases there appears not to be any selectivity, or at least the selectivity for albumins appears to be markedly impaired.

DISCUSSION

Dr. B. K. Hamilton, Baltimore: I would like to ask if the conditions in the blood serum followed the changes which in the chart are shown to take place in the urinary secretion.

Dr. Samuel Amberg: I should like to ask whether Dr. Schlutz found any relation between the urinary manifestations and the stage of the disease; whether globinuria happened only early in the disease or whether it occurred at intervals, and the length of time it continued.

Dr. S. G. Ross, Montreal: It is somewhat aside from the point, but I should like to ask Dr. Schlutz whether, in these cases, he found that there was a consistently low basal metabolic rate. In four such cases that we studied, that is what we have found, and I wonder if it is a constant symptom.

As regards the methods of therapy, we found that the giving of thyroid substance, although it brought the basal metabolic rate to normal, seemed not to have a particular effect on the course of the disease.

Dr. Schlutz (closing): In answer to Dr. Amberg's question, I would say that the condition was intermittent.

These patients were under observation for long periods. The studies were made in four cases. The results are complete in three and two more are now under observation. In two of the cases the study covers a period of nearly one year, and in the other, seven months. There are always periods of exacerbation. We have observed the interesting fact that the patient seems better when the proteinuria is high. This seems almost paradoxic, but nevertheless seems to be true. I do not know what significance to attach to this phenomena.

In answer to Dr. Hamilton's question, a study of the edema fluids has been carried out in some of the cases in connection with the other studies.

In answer to Dr. Ross' question, we did not determine the basal metabolism in these cases but we did use thyroid therapy. We are under the impression that the thyroid therapy is not effective. In one case it seemed to relieve the edema temporarily to a pronounced degree, but this was not a permanent effect.

Fourth Session, 2:30 p. m., May 1, 1928

Postural Reflexes in Relation to the Correction of Improper Position of the Body. Dr. Royal S. Haynes.

In attempting the correction of improper position of the body, the author observed that children without training often performed associated movements of muscles as if the author's plan of reductions was already known. The body seemed to know, before it was taught, what it should do.

Extensor effort in the form of a dorsal kick at the hip threw the hip and knee into extension and inverted the foot in plantar flexion.

Extensor effort in the form of voluntary contractions of the gluteus maximus extended the hip and knee, adducted the thighs and rotated them out and inverted and plantar flexed the feet. The lumbar spine was straightened, the lower abdomen was retracted and the thorax elevated and widened. This was seen in both horizontal and upright positions. In the upright position, these effects straighten apparently bowed legs and correct pronated feet and constitute the "standing mechanism of man." This association was pointed out in the plantigrade position, on hands and knees and in the sitting position when the pelvis is extended.

In the plantigrade position, several natural positions of head and shoulder girdle in relation to flexion and extension of the pelvis were indicated.

A child standing, who drops his head back, extending the lower cervical spine and then leveling the head, flexing the upper cervival vertebrae, shows extensor contraction at hip and knee and inversion of the feet, in addition to other elements of the same mechanism.

The author called attention to the reflex figure in the decerebrate animal, in which reflex augmentation of bone in the antigravity muscles, the extensors of the head, spine, hip and knee permit it to stand as a result of proprioceptive reflexes. The muscles here involved are the same as those of the "standing mechanism." This holds true of the decerebrate child.

The crossed extension reflex seen in the decerebrate animal is seen in part in the child whose kick unconsciously brings about contraction of the muscles of the shoulder girdle.

The analogy was pointed out between the changes in attitude of the decerebrate animal on forcible movement of the head and the unconscious positions of the head in children who make extensor effort in the plantigrade position.

These are due to the tonic neck and labyrinthine reflexes of Magnus and deKleyn, which seem to be brought into action in the movements of the child who brings the standing mechanisms into evidence by change in position of the head.

The similarities pointed out justify the conclusions that the patterns for correction of improper body position exist in the body and may be used if the cortical phasic control of the muscles is developed so that it will aid and not hinder the natural reflex control. The reflex patterns indicate the correct manner for improving body positions.

DR. BORDEN S. VEEDER, St. Louis: I would like to know whether Dr. Haynes uses definite exercises for the contraction of the gluteal muscle in training children with bad posture?

DR. HAYNES (closing): To answer Dr. Veeder's question as to what region of the body I choose to begin my corrective work, I would say that it depends on where the primary defect in motility presents itself. Almost always there is an imbalance in the muscles moving the hip-joint, the psoas and the gluteus maximus. This may be due secondarily to a restriction at the knee or at the ankle due to shortening of the muscles acting on these joints which force a flexion habit at the hip. But almost every patient with improper position of the body shows inadequate extensor control of this joint, which, as I have indicated, is anatomically and biologically of prime importance to the human erect attitude. I have not been able in this communication to bring out the mechanical combinations which result from this inadequacy; but I would like to point out that in studying the subject of improper position, every part of the body must be considered. What affects one part directly affects all the other parts indirectly and every joint and every muscle group depends for its proper functioning on the harmony of the whole structure. It is not a question of method. Many paths may lead to a good result. In investigating this subject, I happened to follow one which seemed to me to be correct from the standpoint of the desired mechanical result, and the observations made of children's actions during their training along this line brought out a composite pattern of associations which can be identified with what the physiologists have found to exist ready-made in all animals for the maintenance of the body in space. So it seems to me that however our individual means for activating the fundamental postural mechanisms may differ, the goal that we should attempt to attain has, ages ago, been set up for us.

SOME FACTORS IN THE INFANT MORTALITY PROBLEM. CHARLES HERRMAN.

The curve of infant mortality has undergone a radical change. The highest point is reached in the spring and the lowest in the summer.

Epidemic catarrh, measles and whooping cough are the chief causes of respiratory infections, and have not been controlled to any great extent.

There has been little if any reduction in the deaths in early infancy. Environmental conditions have little influence on the number of neonatal deaths, which depend primarily on the character of the stock and are largely due to some defect in the germ cells. An extremely defective embryo does not mature, but results in an abortion, miscarriage or still-birth. One less defective may be viable but, being of inferior quality, the individual dies shortly after birth or in early infancy.

Under similar environmental conditions, deaths in early infancy vary with the race and nationality of the parents, that is with the character of the stock. This also determines to a great extent the number of deaths during the rest of the first year.

The limitations of prenatal care should be recognized. Care of the mother during pregnancy and better obstetrics will reduce the deaths due to syphilis, prematurity, the toxemias of pregnancy and the accidents and injuries of labor, but a large number of miscarriages, premature births and still-births and neonatal deaths cannot be prevented by methods now at our command.

A mother who nurses her baby successfully gives it something more than breast milk. Her infant receives not only a superior food, but it inherits favorable unit factors which have a distinct survival value.

Ultimately, the solution of the infant mortality problem, like so many social problems, will depend on preventing the birth of those who are defective physically, mentally or morally.

Nothing in the foregoing paper should be construed as a lack of appreciation of the value of improved environmental conditions.

DISCUSSION

DR. RICHARD M. SMITH, Boston: Dr. Herrman has pointed out two or three points on which I should like to comment, because they call attention to a change of emphasis in the work for the reduction of infant mortality. He said that the reduction in deaths from diarrheal disease had been accomplished primarily by improved hygiene and better feeding. The changes have resulted largely from a social and economic campaign with the assistance of the medical profession, but often not under their direction and frequently in spite of their opposition.

If further reduction in infant mortality is to take place it must be because of better medical practice. Obstetric care must be improved, as Dr. Herrman has said, and the deaths from infectious disease reduced. The reduction of deaths from infectious disease depends on greater knowledge and better medical care.

Although physicians cannot claim much of the glory for the reduction in infant mortality up to now, at this time they should accept the responsibility for a further reduction by improving medical practice, especially in relation to infectious disease.

DR. CLIFFORD G. GRULEE: I should like to call attention to the fact that the New Zealand statistics, which are so frequently quoted, do not take into consideration any death rate among the native population, so far as any one knows, and it is as if the statistics in the United States left out the Negro population and Indian population and said that the death rate was such and such and such and such results were obtained.

DR. WALTER LESTER CARR: I have shown Dr. Herrman statistics from the Manhattan Maternity, a report I received yesterday. During the year there were 1,467 births, and the pathologist's report shows that the neonatal deaths, in which autopsies were obtained, were seventeen. The autopsy records show that prematurity and want of development was the cause of four deaths; meningeal hemorrhage, five deaths; hemorrhagic disease of the new-born, two deaths; atelectasis, asthenic type, two deaths; obstructive aspiration atelectasis, one death; hydrocephalus, one death; congenital heart disease, malformation of the tricuspid and mitral valves, one death; fracture of the temporal bone with meningeal hemorrhage, one death. These were definite influences at the time of birth with a question of intra-uterine nutrition and perhaps a lowered physical condition. In connection with the matter of intra-uterine death, I have a number recorded here, and they include toxemias of pregnancy, torsion of the cord, macerated fetus, anencephalus, hydrocephalus, macerated fetus and hemorrhage.

DR. HOWARD CHILDS CARPENTER: I should like to ask Dr. Herrman why he places pneumonia under the heading of the irreducible deaths of new-born infants. Pneumonia should be considered a preventable disease now that the new-born infants in maternity hospitals have been placed in the hands of pediatricians who will see that they receive proper hygienic care and that adequate measures are taken to prevent their temperatures from becoming subnormal.

DR. ALFRED HAND, Philadelphia: I wish that Dr. Herrman had presented some of the charts showing the birth rates for different communities. It would help in deciding the point that used to be put down as an axiom, that high birth rates and high death rates go together. The subject has some elements in it that are difficult to weigh. One has to be slow sometimes in drawing conclusions.

Great interest can be noted in the fall of diarrheal disease. It has been my experience in the last fifteen or eighteen years to see fewer cases of diarrhea in the wards of the hospitals in the summer than I saw between 1900 and 1910, when a great many cases occurred. It seems to me that Philadelphia was helped by the ordinance compelling all milk sold in the city to be pasteurized. In the summer, the milk tastes as though it were almost sterilized. I think the big milk dealers are careful in the summer to see that the milk is pasteurized. Of course, it seems that the summers are not as hot as they used to be, but it is easier to keep comfortable than in the decades between 1890 and 1910. Life in the city then was intolerable. Now, with the different cooling devices and electric fans and trolleys to cool off on, it is different. In the old days, there was not an electric fan. All those things, I think, come under improved hygiene.

DR. HERRMAN (closing): With regard to pneumonia, I think there is no question that pneumonia now is the most important cause of death in infancy. There is, I believe, no doubt that the majority of the deaths are due to respiratory infection.

With regard to the table showing the conditions that are preventable, I classify all the injuries at birth as preventable. It is not likely that for a great many years there will not be any injuries at birth. As far as pneumonia is concerned, I am not so sure that it can be prevented. To a certain extent it can, but the air cannot be controlled the way milk can. The infant is subjected to that test of respiratory infection, and if it has the power of resistance it can overcome it.

As regards the birth rate, in connection with the better care of infants and the smaller number of offspring, those nationalities which have the highest birth rates will also have the highest death rates, that is a biologic law, the greater the

care, the better the chances of survival, the smaller the number of offspring, but the fact remains that some nationalities have a much lower infant death rate than others.

In regard to the heat of summer, if one takes a series of years the average temperature does not vary. Undoubtedly, the improvement and the decrease in deaths due to digestive disorders is due to the fact that the milk supply has been improved and the mothers instructed in infant feeding and hygiene, that is, conditions that can be controlled, whereas the respiratory infections are difficult to control. Of course, masks can be worn and care taken not to sneeze and cough in the infant's face. But I am not sure that it is possible to prevent a large number of cases of respiratory infection, because one cannot control the condition of the air.

EXAMINATION OF THE BLOOD IN THE NEW-BORN WITH REFERENCE TO TREATMENT FOR HEMORRHAGE. DR. WALTER LESTER CARR.

A study of the bleeding time, clotting time and fragility of the blood in 200 new-born infants was undertaken at the Woman's Hospital to determine, if possible, any factor at birth that might be used for the basis of treatment in cases in which there were clinical symptoms indicating trauma and hemorrhage. The mothers were young and strong, of an average age of 26 years and 2 months. The infants averaged 7 pounds 9½ ounces (3,444.46 Gm.) in weight. The longest labor was forty-five hours and forty minutes and the shortest was ten minutes. The average bleeding time in the normal cases was two minutes and three seconds. in the instrumental cases, the average was one minute and forty-four seconds. The average clotting time in the normal cases was three minutes and five seconds, and in the instrumental cases the average was three minutes and eight seconds. The fragility began in the normal cases at an average of 0.424 per cent and was complete at 0.285 per cent. In the instrumental cases, the fragility began at an average of 0.425 per cent and was complete at an average of 0.295 per cent.

In a comparison of the normal deliveries with the instrumental ones, the blood records do not disclose that prolonged labor, instrumental delivery and cesarean section make any difference in the character of the blood reactions as disclosed in this series. Although the comparison of these observations fails to give definite information for a clinical routine in infants subject to delay and pressure at birth, other groups of infants in which there are symptoms of hemorrhage are under observation.

DISCUSSION

DR. CARR: We are trying to determine if there is a possibility of treatment for injuries at birth with hemorrhage when the injury is in the central nervous system.

FURTHER STUDIES OF PROTEIN FEVER. DR. L. A. HOAG, ELEANOR MARPLES, DR. S. Z. LEVINE and DR. J. R. WILSON.

The studies here reported were designed to evaluate the relative importance of changes in formation and loss of heat in their relation to the etiology of the fever induced by the addition of certain percentages of protein, urea and sodium chloride to the diets of normal infants.

The well-known fact that ingested protein increases heat production has been abundantly confirmed during our study of casein fever. Urea, on the other hand, did not exert a specific dynamic action in the three patients investigated. Distinct

restlessness following the ingestion of hypertonic sodium chloride solutions prevented successful observations as to its effect on the basal metabolism. The published evidence bearing on this point is conflicting.

Another source of extra heat production following the ingestion of these pyretogenetic agents is the increased activity induced in many of the infants. The ingestion of urea produced in one patient an increase in activity (crying, feeding and restlessness while awake) from 40 to 200 minutes a day. Ingestion of sodium chloride by another infant increased his activity from a daily average of 50 minutes to 428 minutes a day. It is our clinical impression that restlessness is not so apparent in infants exhibiting fever of protein origin.

Heat formation may be augmented to some degree by the processes mentioned, but it is evident that fever would not result if there were a similar increase in the loss of heat through the regular channels—vaporization (25 per cent of the total) and radiation and conduction (75 per cent of the total). Vaporization was studied by means of carefully controlled water balance studies designed to determine the amount of water lost from the skin and lungs (so-called insensible perspiration). One infant with a low and poorly sustained urea fever showed a slight decrease in insensible perspiration, from a foreperiod average of about 580 Gm. daily to 523 Gm. in the febrile period and a return to an average of 606 Gm. in the three postfebrile days. Another patient with an average control period output of 633 Gm. of water daily from the skin and lungs lost only 482 Gm. during the day of rather high and well sustained fever induced by sodium chloride. In the postfebrile period the loss of water by these channels rose to an average of 676 Gm. daily. The failure of the insensible perspiration to increase seems of almost as much significance as the somewhat disputable measured reductions.

For the sake of complete accuracy, the possible variations in heat lost by radiation and conduction should also be studied. We plan to do complete heat balances in sodium chloride fever, using a direct heat calorimeter. Even without these data it seems reasonable to assume that in the fevers produced by the pyretogenetic agents studied the primary defect is the failure of the body to eliminate heat as rapidly as it is formed. This in turn may be dependent on the state of "relative thirst" induced in the body by the hydropigenous action of the ingested pyretogenetic agents.

THE CURD AND THE BUFFER IN INFANT FEEDING. DR. JOSEPH BRENNEMANN.
(Read by title.)

A CASE OF TULAREMIA IN A GIRL OF TWELVE YEARS. DR. HENRY DWIGHT CHAPIN.

At the February meeting of the Columbia (S. C.) Medical Society, Dr. Pruitt, the county health officer, read a paper in which eighteen cases of tularemia were reported. He gave a case report of a girl aged 12 years, whom he allowed me to examine a few days later.

Lula L., white, aged 12, presented nothing significant in her family or past history. Her illness began on Dec. 14, 1927, when she was sent home from school complaining of dizziness, prostation, headache, photophobia, nausea and vomiting. Extreme pallor was noted, and the eyes were red and inflamed. That night the temperature reached 103.5 F., and the pulse rate was 128. The child complained of marked dizziness, even while she was in bed. Severe lacrimation was present, and she vomited everything including water. At midnight she complained of pain in the thumb of her left hand for the first time. The thumb was examined carefully, but a lesion was not found at that time. In twenty-four hours a pustule

was present which was incised and a small amount of pus evacuated. In another twenty-four hours the lymph glands in the left axilla were involved; redness, swelling and considerable pain were present. There was some discomfort on the left side of the neck, but lymph glands other than those in the left axilla were not involved.

At the beginning of the third week she complained of severe pain in the left side of the abdomen, so much so that she could not lie on either side; she could not breathe deeply or cough on account of the pain and had to be moved in bed by her mother when a change of position was desired. The spleen was not palpable at first but during the week it became so.

Complete physical examination revealed the following: A marked conjunctivitis with much lacrimation, a small ulcer on the dorsal aspect of the left thumb with inflammation of the left axillary glands; hot and dry skin and brittle hair. The urine examined during the second week was highly colored and had a specific gravity of 1.025 with a trace of albumin. On January 7, the patient had a leukocytosis of 11,000, with a differential count as follows: polymorphonuclears, 50; small lymphocytes, 41; large mononuclears, 7; eosinophils, 0; transitionals, 2 and basophils, 0.

When I examined her the ulcer on her thumb had healed, but the axillary glands were still much enlarged. She was a healthy looking child and did not seem the worse for her illness. A few days before the attack she had dressed two cotton-tail rabbits.

The disease is now fairly prevalent in the United States and is often seen in children. It occurs in nature in ground squirrels, rabbits, rats and other rodents. It is transmitted to human beings in three ways: (1) by the bite of the horse-fly or deer fly; (2) by the bite of the woodtick, and (3) by dressing or dissecting infected rabbits.

Bacterium tularense occurs in culture as bacilli and cocci and has the peculiar property of going through the unbroken skin. It usually produces a small, round, punched-out indolent ulcer, but the disease sometimes occurs when a demonstrable lesion is not present. Four clinical types are recognized: (1) ulceroglandular; (2) oculoglandular; (3) glandular and (4) typhoidal.

The diagnosis may be confused with influenza, typhoid, septic infection and sporotrichosis. The following points may be considered in the diagnosis: the (1) patient gives a history of having dressed or dissected a wild rabbit, or of having been bitten by a fly or tick; (2) the patient gives a history of a primary lesion of the skin, first a papule, then a persistent ulcer, or a primary conjunctivitis followed by ulcers of the conjunctiva; (3) persistent glandular enlargement in the region draining the primary lesion, and (4) fever of from two to three weeks' duration. The diagnosis may be proved by the agglutination test with *Bacterium tularense*.

The treatment is symptomatic.

EXOPHTHALMIC GOITER. REPORT OF TWO CASES IN CHILDREN AGED THREE AND A HALF AND SIX YEARS. DR. DEWITT H. SHERMAN.

In reviewing the literature, I have found reported twenty-four cases of exophthalmic goiter in children under 5 years of age. Mine is the twenty-fifth case. It is possible that the same cases may have been referred to in some instances by different authors.

The youngest was reported by Clifford White as congenital exophthalmic goiter. There is some doubt of the correctness of this diagnosis because of a massive sub-

dural hemorrhage. The next youngest patient, aged 5 months, was reported by Schmauch and referred to by Ochsner and Thompson. Klause reported a case in an infant, aged 9 months; Barrett, one, aged 2½ years; Lahey, one, aged 3 years; Helmholz, one aged 3 years and my case stands next as far as age is concerned. The rest of the cases come within the assumed 5 year limit.

I will emphasize only a few points of my case, which was in a girl, aged 3½ years. Her symptoms were first noticed when she was 2½ years old.

On her mother's side, three ancestors had some thyroid dysfunction, while there were none on her father's side.

Data of her three metabolic tests are completely given in table 1. The first test was made Dec. 5, 1927. On Dec. 12, 1927, her tonsils and adenoids were removed. They were large enough to be a decided handicap, but their section showed only hyperplasia. Her second test was made, Dec. 24, 1927, twelve days after the operation and showed an improvement. The third test was made on

TABLE 1.—*Basal Metabolism in B. P., Aged 3½ Years*

Date	12/5/27	12/23/27	5/20/28
Age	3.6	3.7	4.0
Weight (Kg.)	17.2	17.8	19.3
Standards	Percentage Above Average Normal		
Calories referred to age (Benedict)	50	35	50
Calories referred to weight (Benedict)	24	11	26
Calories per Kg. referred to age (Talbot)	20	3	16
Calories per Kg. referred to weight (Benedict)	29	11	27
Calories per square meter referred to age (Talbot)	26	10	30
Pulse	158-179	106-117	99-111
Blood pressure	130/0	114/0	98/0
Blood Chemistry:			
Urea nitrogen	12.6 mg.	15.4 mg.	
Sugar	74 mg.	93.8 mg.	
Cholesterol	130 mg.		

April 20, 1928, four months later and gave values similar to those of the first test. Consequently, an appreciable beneficial result in the metabolic rate following the operation was not seen.

However, a decided improvement occurred in the blood pressure, pulse frequency and the size of her heart.

The blood pressure was 130 systolic; 0, diastolic, and has gradually decreased to 98 systolic; 0, diastolic. I am surprised to find how infrequently this zero reading of the diastolic pressure in young children is mentioned.

At her first test, the pulse ranged between 158 and 174 but would drop to 130 or 140 when she wakened in the morning. Recently, the pulse rate in the morning has decidedly decreased, the lowest morning reading being 80.

Her heart at first showed some enlargement, the left border being one finger-breadth or more to the left of the left nipple line, and there was a marked systolic bruit heard all over the precordium and transmitted to the left axilla. On the last recent examination, there could be heard only a faint systolic bruit and the heart seemed about normal in size.

Since these cases so frequently come under the classification of status lymphaticus, I appreciated fully the risk of tonsillectomy and adenoidectomy, but felt that the risk was worth while since her condition was becoming progressively worse in spite of skilful management.

Besides other ordinary preliminary safe guarding tests, her blood chemistry was studied and showed nothing unusual except that her blood sugar was low, 74 mg.

Her preliminary operative care was the administration of compound solution of iodine, 5 drops three times daily for two days; 30 cc. of 5 per cent dextrose solution intramuscularly the evening before, orange juice generously during the night, if she was awake, and also in the early morning and a hypodermic of codeine sulphate, ⅛ grain (0.008 Gm.) just before the operation.

The operation was performed by Dr. Clayton M. Brown, with Dr. John T. Evans giving gas with a little ether as the anesthetic.

Nothing could have been more uneventful than her behavior during and after the operation. I am now marking time and noting her progress, with the desire of avoiding further surgical intervention unless her general condition should become worse.

My second case of exophthalmic goiter occurred in a girl, E. M., aged 6 years.

TABLE 2.—*Basal Metabolism in E. M., Aged 6 Years*

Date	2/24/28	4/18/28
Age	6½ years	6½ years
Weight (Kg.)	20.5	21.6
Standards	Percentage Above Average Normal	
Calories referred to age (Benedict)	85	75
Calories referred to weight (Benedict)	74	57
Calories per Kg. referred to age (Talbot)	47	58
Calories per Kg. referred to weight (Benedict)	77	60
Calories per square meter referred to age (Talbot)	85	73
Pulse	172-180	121-133
Blood pressure	130/0	122/0
Blood Chemistry		
Urea nitrogen	17.5 mg. fasting per 100 cc.	
Sugar	95 mg. fasting per 100 cc.	
Cholesterol	167 mg. fasting per 100 cc.	

She was also operated on for removal of the tonsils and adenoids because the local infection was marked. In her, improvement did not occur in any way following the operation. In fact, the right lobe of the thyroid somewhat increased in size.

Table 2 gives her metabolic values, her blood pressure and her pulse frequency before and two months after operation.

DISCUSSION

DR. SAMUEL AMBERG: I wish to cite a case which was interesting. It occurred in a boy, aged 18 months. The father had an exophthalmic goiter and diagnosed his son's condition to be the same. The physician objected to the diagnosis, stating that exophthalmic goiter does not occur in children of that age.

I do not think that much can be expected from compound solution of iodine within two days. It has to be given for a longer period. In Dr. Sherman's case, it seems that the improvement after tonsillectomy was not lasting. Sooner or later, some more stringent measure might have to be taken.

DR. ALFRED HAND: I should like to ask Dr. Sherman if he had any trouble in getting satisfactory estimations with the basal metabolism test. I have had a girl under my observation for the last two years. She was 5 years old when I first saw her. I made a request for the basal metabolism and the report always came back unsatisfactory, indicating that the child did not cooperate. I made an

appointment with the laboratory workers and thought that perhaps I had a little control over the child. When I saw the mouthpiece, I thought it looked rather formidable. The child took it well and got her lips over the flange. As the nostrils were compressed, she would jump around and pull the mouthpiece off. The laboratory workers tried a circular one. She took that and when they compressed the nostrils she would again prevent further operation.

I thought that the difficulty lay in the compression of the nostrils. I suggested something to block the nostrils. I asked her to breathe out and she breathed through the mouth. I told the workers to go ahead and get the mouthpiece in. I put the finger tips over the nostrils without disturbing her, and we got several satisfactory estimations. Her tonsils and adenoids were removed. It was only a temporary effect. The pulse rate decreased. The last time I saw her it was high, but that happened to be during an attack of measles.

DR. SHERMAN (closing): Dr. Amberg spoke of the short time I gave compound solution of iodine in preparing for the operation of tonsillectomy and adenoidectomy. I followed what I believe is the routine procedure in some of the large hospitals in which compound solution of iodine is given for from two to four days as a measure to lessen the surgical risk. These cases are so rare in children that I have had little opportunity to study and carry them through. I consider that the administration of dextrose and levulose was a more important preoperative procedure since the blood sugar was so low.

Any operation in these cases is a great risk, if they belong, as it is claimed, to the status lymphaticus class. But I felt that operation was indicated in both these children for two reasons: first, because the tonsils were so decidedly involved that they would be a serious handicap to any child and second, because infected tonsils have been considered a possible cause of the enlarged thyroids and their hyperactive function.

The younger girl seemed to improve, but the older girl not only did not improve but became worse. Her thyroid is considerably larger, especially on its right side.

Dr. Hand asked me if I had any trouble keeping these children quiet. I did not have the least trouble. The tests were done by our metabolist. The younger child was particularly obedient and cooperative, probably due to the fact that she is mentally capricious and imaginative.

Fifth Session, 9 a. m., May 2, 1928

THE RELATION BETWEEN MALNUTRITION, FATIGUE AND NERVOUSNESS IN CHILDREN. DR. MAX SEHAM.

Nutrition is the process which governs not only the structure, form and size of the bodily tissues and organisms but their functional interactions as well. If for any reason food is withdrawn or digestion and assimilation are interfered with, in order to maintain its temperature, to perform the vital functions of the heart and lungs, to produce mental and physical work, the body will suffer either a compensatory depression in function commonly known as fatigue or an excess in function known as nervousness. Good nutrition or normal nutrition, therefore, may be defined as that physiologic state in which there is an adequate action of all the internal organs, a stable nervous system, good posture, sufficient muscular strength and endurance, well functioning special senses and good inhibition and coordination.

The effect of malnutrition and forced exercise was studied in twenty male albino and hooded rats, ten being used for controls. Throughout the study, each rat was kept in a revolving cage equipped with a pedometer for recording the number of revolutions per day. Each rat was weighed daily before feeding. The rats subjected to malnutrition were fed, during the first eighteen days, bread soaked with milk and a bucket of growing chicken mash. At the end of that period, the diet was reduced to the mash alone, the full diet being continued for the control rats.

The rats were subjected to exercise in revolving cages which were driven by a motor. The exercise lasted for from thirty to sixty minutes at the same time every day. The speed of this exercise varied from fifteen to thirty revolutions a minute. The period of exercise extended over thirty-seven days.

CONCLUSIONS

1. Inanition produces a marked increase in voluntary activity in rats.
2. Inanition produces an increase in blinking, restlessness and irritability.
3. An adequate diet reduces the activity of malnourished rats and causes a simultaneous increase in weight.
4. Forced exercise produces a definite decrease in voluntary activity.
5. Forced exercise produces a loss in gain in weight as compared to normal rats.
6. Forced exercise produces a marked increase in blinking and in restlessness.
7. Rats subjected to forced exercise were not more liable to nasal infections than rats not so subjected.
8. A study of malnourished children suggests that the symptoms of nervousness and fatigue are more numerous in those children whose weight—height index is above 10 per cent than in those whose index is below 10 per cent.
9. The forced feeding rest cure reduces nervous symptoms, increases functional capacity and hastens gain in weight in malnourished children.

DR. CHARLES HERRMAN: I was particularly interested in the tic. Of course, it has been known for a long time that in a person with a tic fatigue will bring out the tic, as stammering occurs under excitement. Several years ago I published a paper on tic and mentioned that it was often associated with scoliosis, due to faulty posture. This fits in well with the experimental work, as undoubtedly a peculiar constitution, with a tendency toward exhaustion and flabbiness of musculature are present, as Stiller described it years ago.

DR. HENRY HEIMAN: Similar experiments have been made on other lower animals, such as the dog. Two years ago I presented a paper on concentrated feeding; previous to that time it was thought that almost any animal could be fattened as long as it was given high caloric feeding, but this was found to be an impossibility. In the literature, Dr. Gibbon experimented on grayhounds and tried to feed them with some concentrated and high caloric feeding, but it was impossible to fatten the grayhounds.

On the other hand, the bulldog can be compared to the lateral type of humanity and the grayhound to the linear type, and one has what is termed a constitutional metabolic aberration in certain children. It is impossible to fatten them, so that they are called today the grayhound type and the bulldog child. There is little difficulty in fattening the lateral type but there is still great difficulty in fattening the grayhound type. Rest was also recommended, and I believe that is an important adjunct in the treatment of all the difficult nutritional cases in the infant.

DR. LAWRENCE T. ROYSTER: I think one loses sight of the fact which Dr. Seham has brought out clearly, that a child can gain at rest on a certain amount of food, but cannot gain on the same amount of food when active. The basal metabolism must be taken into consideration. There is nothing I know of in handling underweight children with the symptoms he intimated, that has the same effect as complete rest.

On the basis of averages, if a child is 15 per cent underweight, it should be put to bed, automatically, because if it does not have the symptoms that are described it is soon going to have them if it is that much underweight. I want to emphasize that not only must it be kept in bed either completely or part of the day but that isolation is excellent.

I have had ample opportunity in experimenting on this; I have adopted a child in my own home who was starved for a long time on account of a stricture of the esophagus, and have followed out my ideas where I could control that child in my own home. The child was much stunted in height, because of improper feeding. In two years, the child grew 11 inches (27.94 cm.). There was an increase in weight. At the age of 7, the child weighed 32 pounds (14.5 Kg., and at the ninth year weighed 72 pounds (32.7 Kg.). I have carried out the procedure accurately in that case and have emphasized not only the complete rest but isolation for the nervous symptoms. Frequently, in doing this, one has to remove the children from the parental influence.

DR. ALFRED F. HESS: What is the chemical composition of the diet? I have more particularly in mind the percentage of calcium.

I have noticed that if rats are put on a diet poor in calcium, they get nervous. The attendants complain about handling them, because they bite so frequently. What was the calcium content of this ration?

DR. CHARLES HENDEE SMITH: A year or two ago some one read a paper before the New York State Medical Society on malnutrition and its treatment. I suggested that the rest cure was the starting point in all severe cases and the most important method of treating these children. The reader of the paper said that he thought it was cruel to punish any child by putting him to bed because he happened to be thin. He said he did not believe in punishing these children.

I mention this to bring out the point that in explaining the rest cure one must make the child think it is a great treat, and have a program that will provide not only rest and isolation but a day which is full of interesting things to do.

DR. H. M. MCCLANAHAN, Omaha: In connection with forced feeding, I wish that Dr. Seham would tell us how he accomplished it. I have prepared a balanced diet, and the mother said that the child would not take it. I should like to know how he forcibly feeds a nervous child.

DR. CHARLES HENDEE SMITH: My plan in forced feeding is to put the food before the child and take it away in half an hour; have him take it or leave it, and in from forty-eight to seventy-two hours he takes it.

DR. SEHAM: In regard to Dr. Hess' point, I was interested in the study only from a quantitative point of view, so I do not know the exact percentage of all the foods.

Regarding the matter of forced feeding, of course I would not presume to suggest to Dr. McClanahan how that ought to be done, but in this particular group reported the children were under the care of nurses. I know that the results at home would be more difficult. The nurses were in charge, either in the home or in the hospital, and from five to seven feedings a day of a highly concentrated diet were given. We allowed between 50 and 75 per cent more,

according to the ages, than the normal diets, and we found that during the first week those children who were in bed ate between 500 and 900 calories more than previously. The average intake was much more than their caloric needs, and what is especially important is that they ate almost one half and sometimes twice as much as they had eaten before they were put to bed. That was rather surprising to me, because I know that the idea prevails that if a child is put to bed his needs also decrease. The large amount of food these children ate was remarkable.

THE RATIONALE OF THE TREATMENT OF EPILEPSY. DR. FRITZ B. TALBOT and DR. HAROLD L. HIGGINS (by invitation). (Read by title.)

THE MONOCYTE IN ACTIVE TUBERCULOSIS. DR. KENNETH D. BLACKFAN and DR. L. K. DIAMOND.

The peripheral blood in twelve infants and children with proved tuberculosis (group 1) and five patients with probable tuberculosis, diagnosed clinically but not proved (group 2), was studied by the supravital technic described by Sabin. The observations in group 1 showed that the activity of the process was reflected in the blood stream by a relative and absolute increase or decrease in the monocytic cells (the mononuclear or transitional cell), a corresponding decrease or increase in the lymphocytes and the appearance in the blood of modified monocytes and epithelioid cells. As examples of the changes observed in the peripheral blood, three cases were given in detail.

In group 2, although the diagnosis of tuberculosis was not confirmed by the usual methods (roentgenograms, tuberculin tests, the finding of tubercle bacilli) the blood changes suggested strongly the presence of infection with the tubercle bacillus as they were identical with the blood changes in the proved cases of tuberculosis.

Fixed smears, stained by the method of Wright, showed an unusual number of abnormal mononuclear cells which are believed to represent modified monocytes and epithelioid cells, as they appear in fixed smears. This opinion is held, as the percentage paralleled the percentage of modified monocytes and epithelioid cells in the supravital stains made from the same puncture wounds and because they reacted differently from the other mononuclear cells—the clasmatocytes (endothelial epithelioid leukocyte, histiocyte or macrophage)—to various staining methods.

CONCLUSIONS

1. The peripheral blood of infants and children with tuberculosis reflects the degree of activity of the process.

2. A high monocytic-lymphocytic ratio and the finding of epithelioid cells usually means an active tuberculous infection.

3. An increasing monocytic-lymphocytic ratio and the persistence of a high absolute monocytic count signifies extension of the process.

4. Reversal of the ratio (a fall in monocytes and an increase in lymphocytes) denotes healing lesions.

5. In cases in which the diagnosis is questionable, blood studies may lead to a correct diagnosis.

6. When the diagnosis is established, blood studies may be of prognostic value in indicating whether the lesion is progressing or undergoing regression.

DISCUSSION

DR. BORDEN S. VEEDER: I should like to ask Dr. Blackfan whether he has had any experience with the blood count in cases in which there is a question of whether the process is tuberculosis or not? For example, in some of the cases of chronic infection of the lung which are seen in older children, is the count of diagnostic value?

DR. B. K. HAMILTON: I should like to ask Dr. Blackfan if he found any parallelism between these changes in monocytes and the intensity of the tubercular reaction?

DR. A. GRAEME MITCHELL: Were these counts always made at the same time of day so as to obviate the factor of fluctuation in counts during the course of the day and such factors as relation to food intake?

DR. MAX SEHAM: I should like to know how Dr. Blackfan arrived at the normal standard for each of these agents.

DR. BLACKFAN (closing): We have under observation a child who had measles and who has an extensive involvement of the lungs. She is 4 years old, with a positive tuberculin test, a normal monocytic lymphocytic ratio, in which we have not been able to find epithelioid cells or modified monocytes. Therefore, we think that she does not have a tuberculous infection. If there are signs of activity due to the tubercle bacillus, I would expect the process to be reflected in the blood stream.

In regard to Dr. Hamilton's question, a girl aged 8 years, was admitted to the hospital in August with the history of loss in weight, fever, cough and epigastric pains. The question of tuberculosis arose, but the roentgenogram was equivocal, and with 2 mg. of tuberculin her reaction was negative. On account of the epigastric pain, a gastro-intestinal roentgenogram was made, which showed a duodenal ulcer. With proper treatment she improved, with disappearance of her symptoms, and went home. She returned a few months later, with recurrence of the former symptoms. On admission, her blood showed a monocytic, lymphocytic ratio of 1:1.2, and the presence of modified epithelioid cells. The tuberculin reaction was still negative, although we have used 6 mg. of tuberculin. Two weeks later, tubercle bacilli were found in the sputum and feces.

In regard to Dr. Mitchell's question, the white blood cells vary from time to time, depending on the time of day and the food intake, but the chief point here, I think, is to detect abnormal mononuclear cells in the blood stream. The ratio with active, advancing tuberculosis has not shown the physiological variations that is usually found in the normal children, although our studies are not complete as yet.

In regard to the standards, we made studies of normal children for different ages, and took these figures and determined an average with our figures and the figures from the textbook of Dr. Lucas and Dr. Griffith, together with figures given by Sabin. These are the average estimated figures.

CERTAIN EFFECTS OF INGESTION OF AMMONIUM CHLORIDE ON THE CALCIUM METABOLISM OF RATS. DR. S. G. ROSS and DR. J. B. SCRIVER (by invitation).

This work was undertaken primarily to elucidate the curative effects of ammonium chloride in infants with tetany. It was a continuation of previous metabolic studies in infants suffering from tetany. It had been shown that ammonium chloride caused an increase in the calcium concentration of the serum in tetany; that it produced acidosis, and that it increased the output of calcium by the kidneys and possibly the excretion of calcium by way of the bowel. In

other words, the effect of this salt seemed to be to mobilize calcium from the body deposits, principally bone, and to draw it into the blood stream rather than to increase the absorption of calcium from the intestine into the body.

Calcium chloride, by analogy, probably acted in the same way by the virtue of its acid-producing effect rather than by the high calcium content. This would explain the inefficacy of nonacid-producing calcium salts such as calcium lactate.

In the present work, rats were used to try to confirm and extend the previous observations. Longer periods of study are possible in experimental animals, which makes it safer to draw conclusions from balance experiments. The pathologic conditions of tetany is reproducible in rats by a low calcium, rickets-producing diet. The rats studied were placed in separate cages in which the stools and urine were collected separately. The food intake was measured. Two types of diet were used: a normal calcium diet containing 630 mg. of calcium per hundred grams of food and a mineral calcium diet containing 6 mg. of calcium per hundred grams of food. Foreperiod collections were made, and then ammonium chloride was given in the food, amounting to 5 per cent of the total food. Experimental periods did not vary between three and ten months. The feces and urine were ashed and their calcium content analyzed. From these figures, the conclusions were drawn.

The effect of ammonium chloride on the blood of rats which had been fed on a low calcium, rickets-producing diet was also studied. Comparison of the calcium content of healthy rats and those which had been fed on a low calcium diet combined with ammonium chloride was also studied.

SUMMARY

When rats are fed on a nominal calcium diet, they eat well and maintain their weight for many months, even after ammonium chloride is added to the diet. The amount of calcium in the feces is much greater than the calcium intake, proving that calcium is excreted by the bowel. When ammonium chloride is added to this diet, there is a definite and persistent rise in the calcium content of the urine. The amount excreted is greater than the calcium intake. The excretion of calcium by the bowel is not increased after ingestion of ammonium chloride. In fact, after a certain period it is decreased.

When rats are fed on a high calcium diet, they eat well and maintain their weight. When ammonium chloride is added to the diet, their food intake is markedly diminished; they lose weight and generally do badly when compared with the rats on a low calcium diet. The amount of calcium in the feces is reduced. The amount of calcium in the urine is increased and parallels the amount excreted by the rats on a low calcium diet.

A low calcium, rickets-producing diet causes a marked reduction in the serum calcium of a rat. This can be definitely increased by the giving of ammonium chloride and has been shown to persist over a period of a month.

The foregoing work shows that calcium is excreted by the bowel, that the administration of ammonium chloride causes a change in the metabolism of the rat, which raises the blood calcium by drawing it from other parts of the body, probably the bone. Part of this calcium is excreted by way of the kidney. There is no evidence that the administration of salt increases the excretion by the intestine. It appears that the excretory function of this organ for calcium is subject to a different mechanism than that of the kidney.

DR. JAMES L. GAMBLE: This paper demonstrates the practicability of metabolic studies in rats. A great deal of qualitative information regarding nutritional

problems has been obtained from feeding experiments with rats. Dr. Ross has shown encouragingly that metabolism can also be studied in these animals in quantitative terms.

His data are the first that ever persuaded me definitely that calcium is secreted by way of the large intestine. I think he has a method of study which will ultimately explain the at present puzzling intricacies of calcium metabolism.

Dr. B. K. Hamilton: The question of whether or not calcium is secreted by way of the bowel is much discussed.

I should like to ask where he thinks the calcium is secreted—in what part of the gastro-intestinal tract? If one feeds an infant or animal a low calcium diet, then, of course, one still has to expect that calcium will be found in the stool, because the gastric juice, the pancreatic juice and the bile, all the secretions of the gastro-intestinal tract, contain calcium. So if calcium is found in the stools of an animal on a low calcium diet, this does not necessarily prove that the bowel is an organ of secretion for calcium.

If parathyroid extract-Collip is given to dogs, there is an increased excretion of calcium with the stools and this shows that the large bowel in dogs is an organ for secretion of calcium. If parathyroid extract-Collip is given to a human being, however, there is an increased excretion in the urine. This shows that the human bowel is not an organ of secretion for calcium. I should like to ask where Dr. Ross thinks the calcium comes from that he finds in the stools of rats on a low calcium diet?

Dr. Alfred F. Hess: I note that the rats Dr. Ross experimented with were adult rats, weighing 250 Gm. or more. I should like to know whether similar experiments were carried out on young rats.

Dr. Ross (closing): With regard to the question of whether calcium is secreted or excreted by the bowel, I am unable to answer that. One of the difficulties encountered when large amounts of calcium were fed and then ammonium chloride added was that there was a definite reduction in the food intake so that it could not be kept constant; this naturally made comparisons on the output in the stools impossible. The other difficulty is the tendency for the stools to contain more water when ammonium chloride is given.

Dr. Hess raised the question as to whether the age of the rat might have an effect on the calcium metabolism. This is undoubtedly true; but here one is primarily concerned not with the amount of calcium absorbed but with the specific effect of the ammonium chloride and only secondarily with the amount of calcium excreted by way of the bowel.

In answer to Dr. Gamble, I can only say that the feasibility of this experiment depends entirely on him, because it was he who designed the cages for this work and, I understand, who is still improving them.

Book Reviews

CONTRIBUTION TO THE CLINICAL PHYSIOLOGY OF WORK IN CHILDHOOD. By W. GOTTSTEIN. Berlin: S. Karger, 1928.

In this book, which is based chiefly on previous publications by Gottstein and Noeggerath, the author presents metabolic data obtained from children before, during, and after work of a standard character. His purpose was to differentiate one type of child from another as regards the efficiency in which they perform and recover from work. Knowing his reaction to work, the author believes that one can, on the one hand, more intelligently select the type of work, profession, or play best suited to the individual; on the other hand, one can give a better prediction as to the individual's probable reaction to disease; on a physiologic basis one can determine for him what restrictions as regards bodily exercise are necessary during convalescence from disease.

Comparing the total ventilation with the oxygen need, the author divided normal children into three groups: (1) those who showed hypoventilation or orthoventilation during both work and recovery; (2) those who showed hyperventilation during work, and orthoventilation or hypoventilation during recovery; and (3) those who showed orthoventilation during work, and hyperventilation during recovery. The children in the first group are very efficient, beginning to recover before the work is completed: those in the second group recover rapidly; while those in the third group recover slowly and are the least efficient.

HIRNTÄTIGKEIT DES SÄUGLINGS. By ALBRECHT PEIPER. Price, 4.80 R. M. Pp. 101, with 22 illustrations. Berlin: Julius Springer, 1928.

This monograph contains a considerable amount of valid material on a period of infancy which has attracted little interest among neurologists or psychologists. In general, the method is that of the psychologic laboratories of some years ago. The observation of various types of sensation with the time of occurrence of each and other similar observations are faithfully recorded.

In the opinion of the reviewer, this work, though interesting and of definite value, is by no means as useful as that of Arnold Gesell. Curiously enough, in a voluminous bibliography, Dr. Gesell's important contributions to the subject are not cited. On the other hand, Dr. Peiper calls deserved attention to the fundamental psychologic work of Magnus and illustrates its importance by admirable photographs.

THE DIAGNOSIS OF CHILDREN'S DISEASES. By E. FEER. Translated by C. A. Scherer. Third edition. Price, $7.00. Pp. 551, with 246 illustrations. Philadelphia: J. B. Lippincott Company, 1928.

The third edition of this standard work, containing additions in illustrations and instructive cases, now makes an excellently illustrated textbook. The book in every way fulfills the requirements of a textbook on the diagnosis of disease in the child. Treatment is not considered except when it is essential for diagnosis. The material presented is treated in a brief and concise manner. Like the other editions, the subject matter does not follow the system used in most textbooks. Instead of following the course of a certain disease, symptoms are described and the disease and conditions in which they occur are enumerated.

THE INTERNATIONAL MEDICAL ANNUAL. A YEAR BOOK OF TREATMENT AND PRACTITIONER'S INDEX. THIRTY-FIVE CONTRIBUTORS, FORTY-SIXTH YEAR. Price, $6.00. Pp. 574, with 86 illustrations and 53 plates. New York: William Wood & Company, 1928.

The present issue maintains the standard of its predecessors. In a year remembered for its advances in many directions, this book contains practically all that is worth while clinically. An attempt is not made to elaborate experimental detail, but the bare working facts of treatment are assembled for the busy practitioner. The plates and illustrations are clear and well chosen. This book makes a handy reference volume on treatment.

Directory of Pediatric Societies

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SECTION ON DISEASES OF CHILDREN

Chairman: Dr. W. A. Mulherin, 753 Broad St., Augusta, Ga.
Secretary: Dr. C. A. Aldrich, 545 Lincoln Ave., Winnetka, Ill.
Place: Portland, Ore. Time: July 8-12, 1929.

AMERICAN PEDIATRIC SOCIETY

President: Dr. Henry L. K. Shaw, 142 Washington Ave., Albany, N. Y.
Secretary: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.

THE ASSOCIATION OF AMERICAN TEACHERS OF THE DISEASES OF CHILDREN

President: Dr. Paul W. Emerson, 86 Bay State Road, Boston.
Secretary: Dr. Ralph M. Tyson, 1527 Pine St., Philadelphia.
Place: Portland, Ore. Time: July 8-12, 1929.

AMERICAN CHILD HEALTH ASSOCIATION

President: Hon. Herbert Hoover, 370 Seventh Ave., New York.
Secretary: Dr. Philip Van Ingen, 370 Seventh Ave., New York.
Place: Stevens Hotel, Chicago. Time: October 15-19, 1928.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. G. R. Pirie, 20 Madison Ave., Toronto.
Secretary: Dr. A. P. Hart, 1844 Bloor St. West, Toronto.

SECTIONAL

CENTRAL STATES PEDIATRIC SOCIETY

President: Dr. H. T. Price, 121 University Place, Pittsburgh.
Secretary: Dr. A. H. Parmelee, 310 S. Michigan Ave., Chicago.
Place: Pittsburgh. Time: October 26-27, 1928.

SECTION ON PEDIATRICS OF SOUTHERN MEDICAL ASSOCIATION

Chairman: Dr. E. C. Mitchell, 1073 Madison Ave., Memphis, Tenn.
Secretary: Dr. A. J. Waring, De Renne Apts., Savannah, Ga.
Place: Asheville, N. C. Time: November 12-15, 1928.

LOCAL

NORTHERN CALIFORNIA PEDIATRIC SOCIETY

President: Dr. W. L. Channell, Medical Bldg., Oakland, Calif.
Secretary: J. E. Parrott, Medico-Dental Bldg., San Francisco.
Place: Various Teaching Schools. Time: Monthly.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Oscar Reiss, Westlake Professional Bldg., Los Angeles.
Secretary: Dr. William Sidney Bowers, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

THE ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. W. Wiley Jones, Majestic Bldg., Denver.
Secretary: Dr. Berryman Green, 537 Republic Bldg., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month, 2:30 p. m., September to May, inclusive.

GEORGIA PEDIATRIC SOCIETY

President: Dr. Joseph Yampolsky, 127 Peachtree St., Atlanta.
Secretary: Nevin M. Atkins, Atlanta.

PEDIATRIC SECTION OF FULTON COUNTY MEDICAL SOCIETY, ATLANTA, GA.

President: Dr. William W. Anderson, 362 Peachtree St., Atlanta.
Secretary: Dr. Lee Bivings, Exchange Bldg., Atlanta.
Place: Academy of Medicine, 32 Howard St., Atlanta.
Time: Second Thursday of each month from October to April, at 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. James Herbert Young, 66 Commonwealth Ave., Boston.
Secretary: Dr. Thomas Lanman, 286 Marlborough St., Boston.
Place: Boston Medical Library. Time: Second Friday of each month.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Maurice Blatt, 30 N. Michigan Ave., Chicago.
Secretary: Dr. J. K. Calvin, 104 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. L. R. De Buys, 1487 Delachaise St., New Orleans.
Secretary-Treasurer: Dr. C. T. Williams, 7401 Burthe St., New Orleans.

DETROIT PEDIATRIC SOCIETY

President: Dr. George E. White, Capitol Theatre Bldg., Windsor, Ontario, Canada.
Secretary: Dr. W. S. O'Donnell, 1563 David Whitney Bldg., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. F. W. Schlutz, University of Minnesota, Minneapolis.
Secretary: Dr. E. S. Platou, 730 La Salle Bldg., Minneapolis.
Place: University Campus and Rochester. Time: Winter, Spring, Summer, Fall.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. Park J. White, Beaumont Bldg., St. Louis.
Secretary-Treasurer: Dr. Ralph L. Cook, 508 N. Grand Blvd., St. Louis.
Place: St. Louis Children's Hospital. Time: At least once a year and contingent thereafter on the arrangement of a suitable program.

NEBRASKA-IOWA PEDIATRIC SOCIETY

President: Dr. Floyd Clarke, 731 City Nat'l Bank Bldg., Omaha.
Secretary: Dr. R. B. Eldredge, 1036 Medical Arts Bldg., Omaha.
Place: Add-Sell Restaurant. Time: Second Thursday of each month from October to May, inclusive, 6 p. m.

BROOKLYN PEDIATRIC SOCIETY

President: Dr. Louis M. Ruderman, 961 Eastern Parkway, Brooklyn.
Secretary: Dr. Joseph F. Paulonis, 1357 Bushwick Ave., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

BRONX PEDIATRIC SOCIETY

President: Dr. William Hinz, 1964 Grand Concourse, New York.
Secretary: L. H. Barenberg, 1749 Grand Concourse, New York.
Place: Concourse Plaza, 161st St. and Grand Concourse, New York.
Time: Second Wednesday of each month, except June, July, August and September.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady, N. Y.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany, N. Y.
Place: Various Cities in New York. Time: Fourth Thursday of October, January and April.

PEDIATRIC SECTION OF THE NEW YORK ACADEMY OF MEDICINE

President: Dr. Stafford McLean, 17 East 71st St., New York.
Secretary: Dr. Frank Elmer Johnson, 300 West End Ave., New York.
Place: New York Academy of Medicine, 2 East 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

ROCHESTER PEDIATRIC SOCIETY

President: Dr. Paul W. Beaven, 26 S. Goodman St., Rochester, N. Y.
Secretary: Dr. Edwin R. Reynolds, 1620 St. Paul St., Rochester, N. Y.
Place: Arranged by Program Committee. Time: First Friday of each month from October to May.

THE PEDIATRIC SECTION OF THE ACADEMY OF MEDICINE OF CLEVELAND

Chairman: Dr. J. W. Epstein, 3912 Prospect Ave., Cleveland.
Secretary: Dr. Charles W. Burhans, 14805 Detroit Ave., Lakewood, O.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

PEDIATRIC SECTION, ACADEMY OF MEDICINE, TORONTO

President: Dr. M. A. Cox, 34 St. Clair Ave. West, Toronto.
Secretary: Dr. F. R. Hassard, 1361 King St. West, Toronto.
Time: November 17, December 15, February 16 and March 15.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Edward L. Bauer, Jefferson Medical College, Philadelphia.
Secretary: Dr. John Porter Scott, 2040 Pine St., Philadelphia.
Place: College of Physicians, 19 S. 22nd St., Philadelphia. Time: Second Tuesday of each month from October to June, inclusive.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. W. D. Blue, 1024 Madison Ave., Memphis, Tenn.
Secretary: Dr. Gilbert J. Levy, 899 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

TEXAS PEDIATRIC SOCIETY

President: Dr. Edwin G. Schwarz, Medical Arts Bldg., Forth Worth.
Secretary-Treasurer: Dr. Ramsey Moore, Medical Arts Bldg., Dallas.
Place: San Antonio. Time: October, 1928.

RICHMOND PEDIATRIC SOCIETY

President: Dr. T. D. Jones, Medical Arts Bldg., Richmond, Va.
Secretary: Dr. W. Ambrose McGee, West End Medical Bldg., 2618 Grove Ave., Richmond, Va.
Place: Westmoreland Club, 601 E. Grace St., Richmond, Va.
Time: First Thursday of each month (other than during the summer).

VIRGINIA PEDIATRIC SOCIETY

President: Dr. Lawrence T. Royster, University, Va.
Secretary: Dr. William B. McIlwaine, Petersburg, Va.
Place: Danville, Va. Time: October 17, 1928.

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. E. D. Carder, 736 Granville St., Vancouver, B. C.
Secretary and Treasurer: Dr. George A. Lamont, 736 Granville St., Vancouver, B. C.

SEATTLE PEDIATRIC SOCIETY

President: Dr. George B. McCulloch, Cobb Bldg., Seattle.
Secretary: Dr. C. L. Smith, Stimson Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, at 7 p. m.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. A. B. Schwartz, 418 E. North Ave., Milwaukee.
Secretary: Dr. M. G. Peterman, 167 Seventeenth St., Milwaukee.
Place: Children's Hospital, Milwaukee. Time: Second Wednesday of each alternate month, beginning with February.

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CONTENTS OF PREVIOUS NUMBER

SEPTEMBER, 1928. NUMBER 3

Permanent Records of Growth and Nutrition of Children. H. D. Clough, M.D., and John R. Murlin, Ph.D., Rochester, N. Y.

Uveoparotid Fever as a Manifestation of Mikulicz's Syndrome. Louis P. Hamburger, M.D., and Alexander J. Schaffer, M.D., Baltimore.

The Use of Dextrose Intraperitoneally in Infants and in Young Children. Clifford G. Grulee, M.D., and Heyworth N. Sanford, M.D., Chicago.

Factors Influencing the Excretion of Calcium. Bengt Hamilton, M.D., and Margaret Moriarty, B.S., Boston.

Treatment of Fusospirillary Infections of the Mouth in Children, with Special Reference to the Intramuscular Administration of Sulpharsphenamine. Harold K. Faber, M.D., San Francisco.

The Respiratory Metabolism in Infancy and in Childhood: IX. The Respiratory Exchange in Marasmus; Carbohydrate Metabolism of Normal and of Marasmic Infants with and Without the Administration of Insulin. James R. Wilson, M.D.; Samuel Z. Levine, M.D., and Gertrude Gottschall, B.A., New York.

The Rôle of Hemolysis in Jaundice of the New-Born Infant. John McKenney Mitchell, M.D., Bryn Mawr, Pa.

Diabetes Mellitus in Children. Studies of the Height and Weight of Forty-Five Patients. Harvey Spencer, M.D., Boston.

Case Reports:

Actinomycosis of the Lung: Report of a Case in Which Bronchoscopy and Injections of Iodized Oil 40 Per Cent Were Used. F. Elmer Johnson, M.D., and John Devereux Kernan, M.D., New York.

Meckel's Diverticulum with Hemorrhage. M. G. Peterman, M.D., and S. J. Seeger, M.D., Milwaukee.

Dipylidium Caninum Infection in an Infant Six Months of Age: Report of a Case. Harold C. Stuart, M.D., and Donald L. Augustine, Sc.D., Boston.

Progress in Pediatrics:

The Bacteriology and Serotherapy of Measles: A Historical and Critical Review of Literature on Experimental Aspects of Measles. Katsuji Kato, M.D., Los Angeles.

Pediatric Biographies:

Felix Würtz. John Ruhräh, Baltimore.

News and Comment.

Abstracts from Current Literature.

Society Transactions:

American Pediatric Society.

Book Reviews.

Directory of Pediatric Societies.

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